

VOLUME 4
(Old Series, Vol. IX)

MAY, 1931

NUMBER 11

ANNALS OF INTERNAL MEDICINE

PUBLISHED BY

The American College of Physicians

CONTENTS

	PAGE
Trauma to Viscera from Non-Penetrating External Injuries, with Special Reference to the Heart. E. L. TUOHY AND P. G. BOMAN.....	1373
Chronic Meningococcemia without Localizing Signs. S. S. RIVEN AND A. A. APPLEBAUM	1387
Non-tuberculous Spontaneous Pneumothorax. R. L. FISHER.....	1395
Cardiac Overaction: The Most Constant and Dependable Sign in Thyroid Toxicity. H. J. VANDEN BERG.....	1406
The Pituitary and Suprarenal Cortex as Related to Pigment Formation. ROBERT P. MOEHLIG.....	1411
Thoracic Aneurysm. SHELTON P. SANFORD.....	1417
Chronic Pulmonary Infections in Childhood. ALLEN K. KRAUSE.....	1424
The Effect of Sodium Malate Combinations upon Gastric Acidity. J. C. KRANTZ, JR. AND A. A. SILVER.....	1441
Tuberculin Therapy. MILES J. BREUER.....	1447
Present Status of Heliotherapy in Tuberculosis. C. K. PETTER.....	1452
Mild Hyperthyroidism and the Neuroses. PHILIP S. SMITH.....	1460
Scurvy in the Presence of Thyrotoxicosis. R. H. KAMPMEIER.....	1469
Editorials	1472
Abstracts	1482
Reviews	1484
College News Notes	1486

Issued Monthly
ANN ARBOR, MICHIGAN

A New Monograph!

THE RENAL LESION IN BRIGHT'S DISEASE

THOMAS ADDIS

Professor of Medicine, Stanford University

JEAN OLIVER

*Professor of Pathology, Long Island College of
Medicine; Formerly Professor of Pathology,
Stanford University*

WITH 170 FULL PAGE PLATES (2 IN COLOR)

21 TEXT ILLUSTRATIONS AND 1 LARGE FOLDING CHART

A new and entirely original monograph on Bright's Disease, describing new methods for the determination of the nature and extent of the renal lesion in Bright's Disease applied during the life time of a series of patients. The original experimental basis of these methods is reviewed and the details of the clinical application given. The methods are applied to seventy-two cases, which cover all the various forms of the disease.

4TO, CLOTH, 640 PAGES, 170 FULL PAGE ILLUS. (2 IN COLOR),
21 TEXT ILLUSTRATIONS, LARGE FOLDING CHART \$16.00 net

Complete Catalogue and Circulars on Request

PAUL B. HOEBER, INC., PUBLISHERS

SEVENTY-SIX FIFTH AVENUE, NEW YORK, N.Y.

*Publishers of The American Journal of Surgery; Annals of Medical History;
Annals of Roentgenology; Clio Medica, etc.*

Trauma To Viscera From Non-Penetrating External Injuries, With Special Reference To the Heart*

By E. L. TUOHY, B.A., M.D., F.A.C.P., AND P. G. BOMAN, B.A., M.D.,
Duluth, Minn.

RUPTURE of hollow viscus abdominal organs readily follows in man external blows, such as kicks by animals, falls from heights, or viselike compression between moving vehicles or cars. It is not so generally known that similar ruptures and tears can likewise occur to the thoracic contents. Twenty years ago such accidents occurred chiefly on farms or attended the lumber industry; today the automobile, the aeroplane, the erection of skyscrapers and general industrial activity, have expanded such injuries to an appalling extent. The great weight and high speed of automobiles, not to mention the momentum attained by falling aeroplanes, create terrific force, difficult to appreciate. A small car has been known to hit a heavy reinforced concrete bridge, shearing off its concrete side wall for several feet as if with a giant knife. The force is comparable in some degree, at least, with that of a tornado which blows straws into a tree!

An active autopsy and pathological service at St. Mary's hospital, Duluth,

and certain affiliated institutions, has yielded well over one thousand autopsies in a time period of about three preceding years. In this list there is an ever increasing number of road accidents in which chest and abdominal† injuries, with or without skull, rib, spine and extremity fractures, abound. We wish to draw upon certain of these experiences for illustrative material presented in this paper, and particularly to call attention to serious internal damage to the heart and lungs and other viscera without external bruising, consequential laceration or bony fractures.

The subject is far from a new one. The student of medical history finds that mediaeval surgery dealt much with battle injuries, as did Paré; but even without association with Mars, a rack-teering age, when every man was his own defender, invited rough tactics. Moynihan's reference to early surgery

†Lacerations and tears have been found in almost every intra-abdominal organ except the stomach and large bowel. Incidentally, even where extensive fractures occur (including the skull) the fractures are less a lethal factor than general concussion and shock. Shock receives too little immediate attention. Too many delay in the receiving room for X-ray films of doubtful quality as well as utility.

*From the Department of Medicine, The Duluth Clinic, Duluth, Minn. Read in abstract only before the Minnesota Society of Internal Medicine, Nov. 11, 1929, St. Paul, Minn.

on the protruding spleen following a butcher knife stab illustrates the point. In reference to chest injuries, Hirschfelder's¹ book on "Diseases of the Heart and Aorta" gives a good review, and contains useful references. Kugel² in 1909, instanced a 44 year old man who was hit by a heavy falling bale of goods. Immediate prostration and severe pain followed, with revival after stimulants, but death at the end of forty-two hours. At autopsy a rupture was found in the right auricle. One of the writers (E.L.T.), together with Dr. George Berdez^{3*}, in 1926 re-

ported "two instances of perforation of the heart following non-penetrating chest injury." These illustrated the contrast between early death from ventricular rupture, and delayed death after a beginning repair in a heart wall laceration. There is much more in the literature on immediately fatal cases of rupture than on functional perversions appearing after such injuries. Much interest centers about a report on the subject by the Kahns (Maurice H. and Samuel)⁴ published in April, 1929. Their article has particularly great industrial interest. While there is no autopsy confirmation of some twelve cases presented, the clinical data are clearly given, and there are some fifty-five literature references. The authors discuss the results on cardiac function (notably rhythm and conduction alterations) after direct and indirect chest injuries inducing "contusion and concussion," concluding rightfully that on these matters the present literature is quite meagre.

We may proceed, therefore, with the knowledge and the certainty that just as the abdominal organs† suffer tears

*The original report includes the data, history and autopsy findings. Photomicrographs are shown of the area of rupture in a 63 year old man, who two weeks before death had been in an auto collision and was thrown unexpectedly and forcibly against the steering wheel of his car. The blow was sufficient to twist the wheel. Despite this and a good deal of faintness, he got about, but "felt faint frequently and vomited almost daily." He appeared to be getting better, when he gasped suddenly in a deep laugh while witnessing the silent film of Harold Lloyd in "The Freshman," and was carried out of the theatre dead! No external abrasions or fractures were found. He had had a tear and laceration near the apex into the wall of the left ventricle. Sections showed clearly fragmented muscle fibres, old hemorrhage and granulation tissue. The ventricle ruptured through at this point. He had generalized arteriosclerosis, with some of the coronaries, but both were patent in their main branches.

The other instance was that of a boy aged 11. He was brought into the hospital a few minutes after being struck by an automobile. Restoratives brought back some radial pulse. He died three hours after entering the hospital. The pericardium was greatly distended with blood. The heart (otherwise normal as to valves and muscle) had a small opening, just admitting a match, into the left ventricle near the apex. (It is stated by

physiologists that even with heart rupture the organ carries on until the pressure outside of the chambers in the pericardial sac equals that within, when contractions cease. This likely is the reason for the need of early surgery in suspected chamber leakage after injury, and the explanation of increasing recoveries after skillful suture).

†Liver tears are not uncommon after external trauma. Dr. Angus Cameron, Minot, N. D. showed one of us (E.L.T.) the instance of a 3 inch tear into the liver occurring to a 4 year old child after the impact of the horn of a cow swinging back and hitting the youngster as he stood by his mother while she was milking. We have seen a 5 year old boy, badly mangled in an auto-

and contusions so also the same type of trauma may damage the contents of the thorax. Since not all of these result fatally at once, or death is postponed some time, it seems fair enough to enter into a cautious discussion as to the possible functional disturbances, particularly of the heart, that may result after injury, and in these non-fatal cases it is possible that we may find an explanation of certain aftermaths of injuries that we erroneously label cardiac or compensation neuroses.

As to the mechanism of hollow viscus damage after injury, all writers agree with Hirschfelder¹ upon the influence of unchecked and unexpected force expended at a time when a contracting muscled organ, full or partly full of near liquid contents, is suddenly compressed. There is in the literature much repetition of such accidents as falls from heights to hard surfaces or to water; planks or cases being pulled or tipped upon the worker; cars slipping off supports and jacks, settling upon the victim with great force; truck handles or squeezing injuries between rigid walls or moving cars—all providing infinite variety.*

mobile accident, where death resulted from severe skull fracture and brain concussion. Despite the fact that he had no abrasions over his liver area (and indeed, the liver capsule itself was unbroken) there was a large area in the middle of the right liver lobe extensively crushed and lacerated, with resultant hemorrhage. It is well to recall that this type of liver injury, where the patient survives, is often followed by extreme hyperpyrexia.

*Our autopsy service has produced two instances of rupture of the aorta itself, but they are not included in this report because almost no clinical data were preserved with the records.

The Kahns'⁴ article introduces certain criteria bearing upon the question of relation of disability and injury to compensability. While this matter of compensability need not have intimate relationship to demonstrable pathological sequences, and is more a legal than a medical assignment, yet much of our vaunted "science of medicine" is based on empirical experiences no better founded than subjective disability and incapacity from usual work. Naturally this kind of evidence is materially strengthened when objective data, such as arrhythmias, changes in heart outline or in electrocardiograms, are available. In effect, these are the Kahns' statements:

1. From the standpoint of labor and compensation a man is healthy if he has been able to work for a long period without distress or long interruption.

2. If such a man has a direct or indirect violence applied to the chest and develops incapacitating cardiovascular states, these must be considered to have arisen from an aggravation of a previously existing asymptomatic condition or arisen from damage to a previously normal heart.

3. There must be prompt development of symptoms: "Pain, with its concomitant dyspnea, rapid, irregular pulse, faintness, prostration, cold sweats, etc., in order that casual or aggravating relationship be clearly established." Recurrence of symptoms after temporary improvement is said to be attributable to the original injury. (While such dicta are a good basis of discussion, they cannot be taken as final criteria. For example, most of the sudden signs mentioned under paragraph 3 can arise from basal brain in-

juries, without especial chest localization.)

Localizing evidence in terms of heart outline and contours, demonstrable perversions of rhythm and conduction, decisive evidence of heart incompensation, lend increasing certainty in living clinical cases, the victims of chest injury. There still remain two fields in which our impressions and surmises in terms of their trauma offer interesting speculation. We refer to the group with previous cardiovascular disease (chiefly sclerotic changes yielding the background for rhythm and conduction disturbances), and the functional group that must closely border upon traumatic neuroses. We may state that neuroses, while occurring at all ages, are more characteristic of the young, and arteriosclerotic phenomena of the ageing. Therefore, an instance of auricular fibrillation, occurring in a truck driver aged 20 (reported by Levison⁵, has unusual bearing on this subject. This young man, after a severe crushing injury of his thoracic region, developed severe pain over the precordium, accompanied by violent dyspnea, but without cyanosis. There was a marked pulse deficit (the rate was something about 150). No electrocardiogram was taken until some thirty-six hours later, when normal rhythm had been restored. Levison discusses the question of liability and the relation of auricular fibrillation to an individual's capacity. Bearing upon the question of the previous status of the heart, he observed that most individuals, while they may not be conscious of a recently developed auricular fibrillation, state on questioning that their

capacity has been suddenly and decidedly reduced.

The Kahns⁴ also report the instance of a well nourished man of 33, who was hit by a heavy plank falling on his chest from a height of about eighteen feet. "During two weeks of hospital observation he felt weak, with pressing pain across the front of the chest." Some three months later his heart was not enlarged, but an electrocardiogram showed coarse auricular fibrillation with tachycardia. Quinidine sulphate promptly restored normal rhythm. They stated that no such condition as rheumatism, syphilis or arteriosclerosis, Graves' disease or toxic agents, could be shown to have any connection with his illness; and the size of the heart precluded previous valvular or pericardial disease or a hypertensive background.

One of us (E.L.T.) saw in consultation a 36 year old man in January, 1926, who had an obvious auricular fibrillation.* Two days previously he had been hit on the chest by the heavy limb of a falling tree. Because of an associated nervousness, coarse tremor, and some slight enlargement of his thyroid, he was studied from the standpoint of a possible instance of hyperthyroidism, influenced by the shock of his injury. He had no weight loss, there was no unusual feeling of bodily warmth, and several basal metabolic readings were within normal limits. We ruled (possibly erroneously) that his injury had no connection with his heart situation, and the man passed out from under observation.

*"Paroxysmal auricular fibrillation" must always be considered in these etiologic problems.

The question is immediately presented, if we do attribute these instances of auricular fibrillation to injury as to where the damage occurs to the heart and what is its general nature. Are we dealing with laceration, hemorrhage, edema, or lesser grades of concussion, such as are better understood in terms of damage to the cranial contents? This question, particularly related to hemorrhage, assumes an even greater position of importance in terms of heart block in conduction disturbances.

C. Theim⁶ in his handbook of diseases due to accidents, instances the case of a beer deliverer who was kicked in the left chest by a horse. He retained for fourteen days a feeling of substernal oppression, with a sense of impending death, and had some pain distribution down the left arm. Fifteen months later he died in an anginal seizure. The interventricular septum showed definite evidences of old hemorrhages, with resulting scar. It was concluded by the reporters of the case that there had been a hemorrhage induced into the interventricular septum, leading to a conduction disturbance. Unfortunately, no clinical data accompany the report which would help to determine the type.

We have closely studied a male 70 years old, who for many years carried on efficiently as an employee of a department store. Some of his duties involved the carrying of heavy sacks of material weighing as much as one hundred pounds. These he usually lifted to his shoulder, and he managed to do so without undue fatigue, dyspnea or distress. On Aug. 6, 1928, he tripped and fell on a stairway in such a manner as to hit his thorax a stun-

ning blow. There was immediate pain, rather generally through the chest, chiefly about the left side. While he was stunned he was not unconscious. Breathing deeply did not greatly increase his pain. There was an impression after bringing him to the hospital that there might have been a cracked rib, but no fractures nor displacements were found. He remained in the hospital only three days, but on returning home he continued to have persistent discomfort over the precordium, and had to get about quite cautiously. On his return to the hospital Sept. 10, 1928, an electrocardiographic study (Fig. 1) made by one of us (P.G.B.) showed a complete heart block. Five weeks later, on re-examination, he had normal sinus rhythm, but right bundle branch block (Fig. 2)—this condition lasting for about ten or twelve days, when the complete block returned, together with the evidence of the right bundle branch block—and this has remained up to date (Fig. 3).

This 70 year old man has plenty of evidence of generalized arteriosclerosis. What was the relationship of his injury to this decisive interference in his conducting mechanism? The answer could be more dogmatically given could the interventricular septum be carefully examined grossly and microscopically within the few weeks after the onset of his block. Fortunately, however, he has continued to live, and we are forced to enter upon a certain degree of speculation.

Two general hypotheses present themselves: This 70 year old man came by his conduction disturbance through the usual route of myocardial fibrosis, with localization in the interventricular

septum and affecting the bundle of His, independent of his injury; or, the injury induced traumatic sequences, the most likely of which is hemorrhage into the same area. Premortem hemorrhage into this area of the bundle of His is not uncommonly divulged at

postmortem. We recall the instance of a man dying from brain tumor who showed such a hemorrhage that must have precipitated his death.

Lubarsch⁷ discusses this important issue of hemorrhage into the heart muscle in various regions, commenting

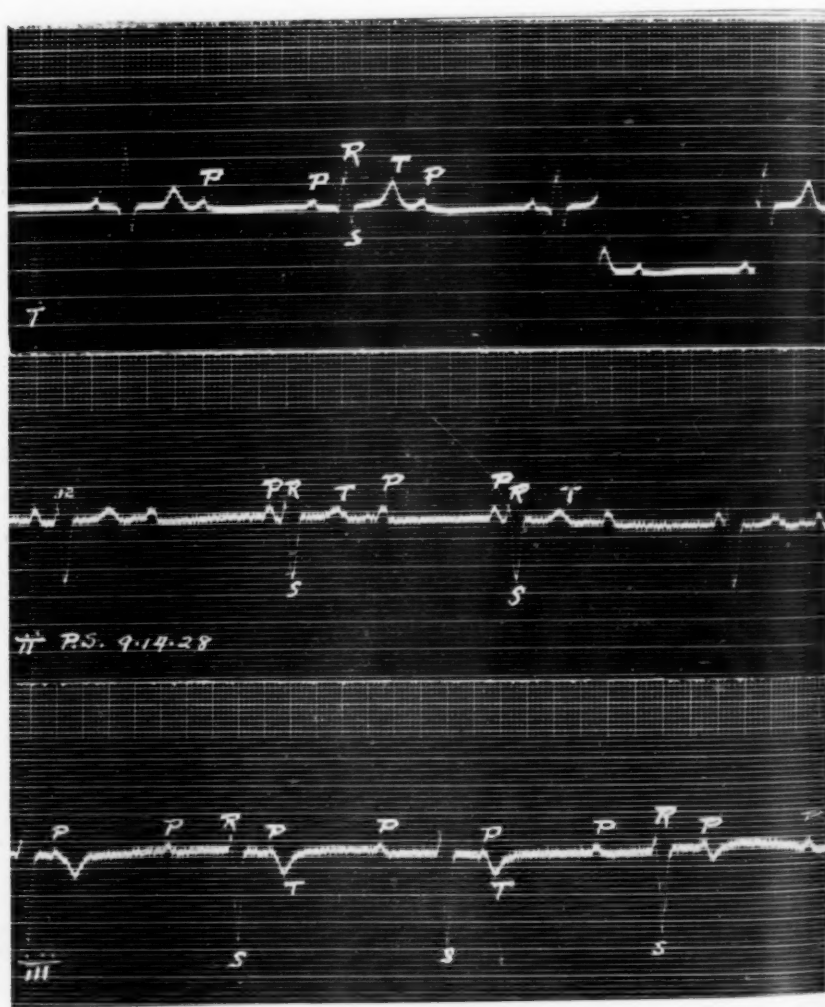


FIG. 1. Electrocardiogram shows a complete atrioventricular block, with an auricular rate of 70 and a ventricular rate of 35. The Q.R.S. complexes indicate either an incomplete bundle branch block or the possibility that the ventricular pacemaker is located in the left branch of the bundle of His. The T-wave shows normal amplitude in Lead I, a moderate reduction in Lead II, and inversion in Lead III.

upon the well known local and constitutional active and predisposing states. Naturally, the signs and symptoms must vary greatly, dependent upon the site where exudation occurs: the junctional tissues yielding a maximum of conduction disturbances even with

very limited areas involved; rhythm and rate disturbances following readily upon invasion of areas about the sinus and sino-auricular node.

Particular interest centers about the interventricular septum in terms of the greatly increasing knowledge and lit-

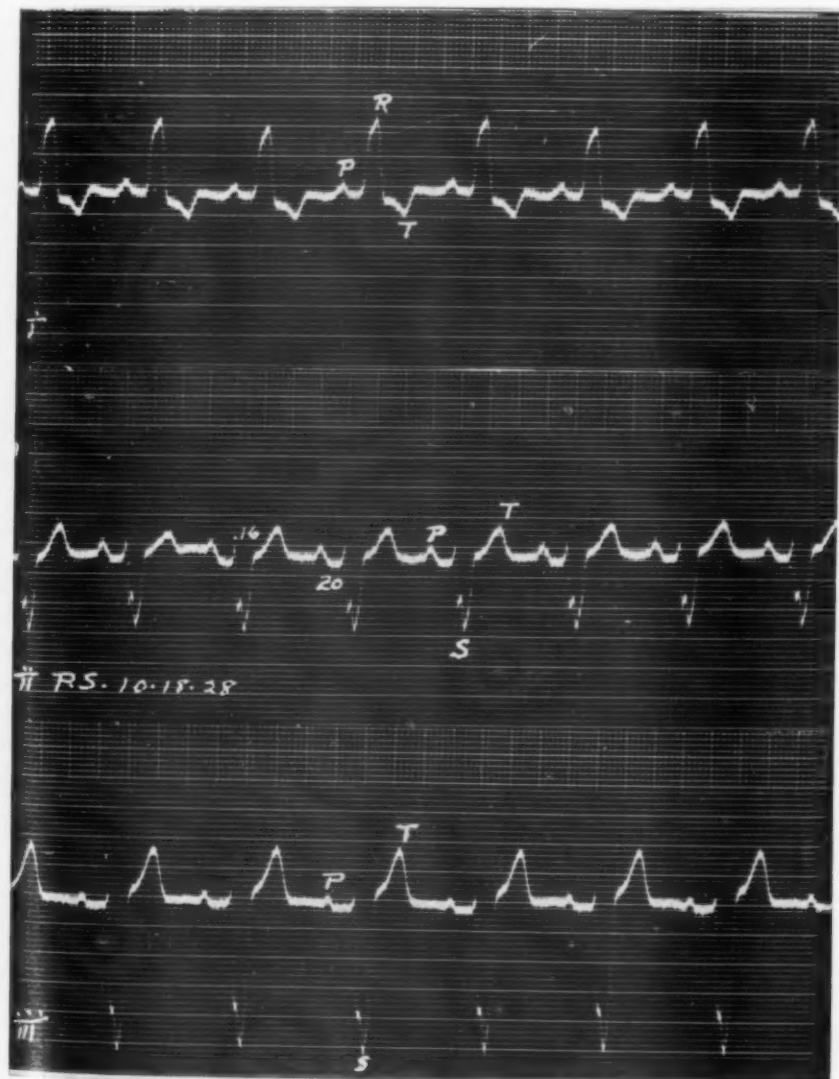


FIG. 2. Record shows a normal sinus rhythm, with an auricular and ventricular rate of 70. A complete right bundle branch block is present.

erature on the coronary blood supply to the heart and its normal variations. Whitten's⁸ injection and corrosion methods in studying heart vasculature, have conspicuously helped in identifying the normal, with its variations, as

well as the abnormal and its anastomotic possibilities. The application of this knowledge has been found in the sequences known to follow infarction in the main division of the coronaries. T-wave studies by many English and

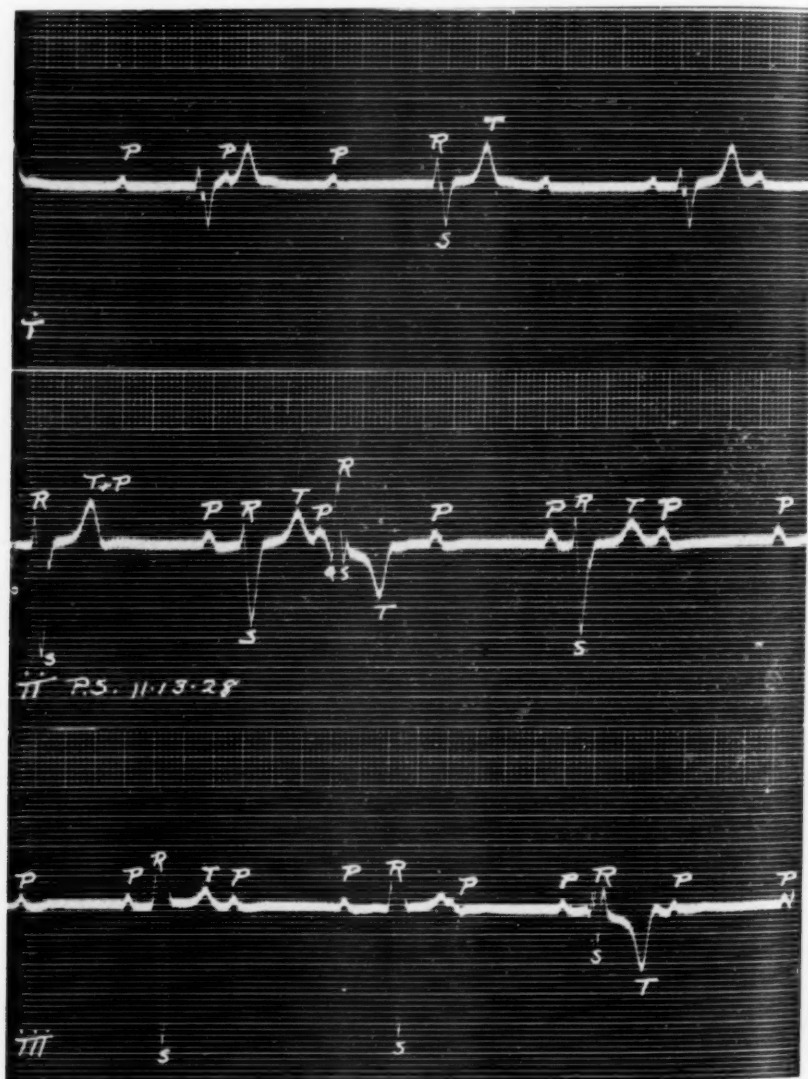


FIG. 3. This record shows a return of complete heart block, with complete auriculoventricular dissociation. The ventricular rate is 38 and the auricular rate 80 contractions each minute. Right ventricular extrasystoles are noted. (This record is very similar to that shown in Fig. 1, except that the T. wave is upright in Lead III).

American authors^{9 10 11 12 13 and 14}, with especial references to the variations in the ventricular complexes in established cases of myocardial infarction and fibrosis, while not yet yielding us unvarying characteristic forms, still have greatly expanded cardiac lesion localization to something comparable with brain localization in terms of motor and sensory phenomena. While it cannot be stated without reservation that the absence of characteristic ventricular complex changes in our patient rules out infarction, still the evidence is strongly corroborative that it did not exist. As a matter of fact, the clinical evidence admits of finer differentiation even than does the pathological. The distinction between infarction and hemorrhage into tissues is one of degree, because the events of infarction leading up to anemic necrosis or connective tissue replacement include early hemorrhagic infiltration into the infarcted area. We may simply state that the electrocardiographic evidence in our man gives no hint as to infarction. He has had no evidence of syphilis, and only moderate hypertension. Something happened to him to give him his total heart block, but it was not fully established until sometime after our observation began. The evidence is clear that a shifting status as to degree and type supervened: a total heart block, followed by a period of branch bundle block, to be later followed by a combination of both. We consider this of some importance as indicating that his complete block was not the result of a fixed pathological lesion, but gradually became so. Hemorrhage could explain this sequence, even as it did in C. Theim's⁸ report of the case

of the man kicked in the chest by a horse.

In fortunate contrast to this instance of an elderly man we have full data upon an apparently otherwise healthy man, aged 43, as follows:

Mr. D. A., while in a stooped position, lifting a very heavy manhole cover in the street, felt immediately faint; soon he "began to sweat profusely and there was a pain across the chest, down into the left arm." This only lasted a few minutes. He pulled himself together and finished out his afternoon's work, but felt very poorly. The following morning, after breakfasting and attempting to leave his house, he stopped on the sidewalk with a great sense of weakness, dizziness and a feeling of impending disaster. He remembers that there was soon a feeling as of impending movement of his bowels, and then he fainted. Fifteen minutes later a physician saw him, and stated that "his pulse was very slow (down to about 26)." That day and the next the pulse gradually came up to 50 and 60, but he continued to be extremely dyspneic, and found it almost impossible to lie down or sleep.

When brought to us a week after his strain he appeared very ill: pallid, slightly cyanosed, rapid shallow breathing, and an anxious appearance. Taking his pulse at the wrist there were occasional dropped beats, but the others seemed fairly evenly spaced. The neck veins were markedly overfilled; the liver edge pushed down and felt rounded; there were many non-resonant râles at the bases of the lungs. The heart outline was extended moderately to the left. Three tones were distinctly heard at the apex (splitting of the first tone?), and there was a short, puffing systolic murmur. Branch bundle block was suspected. The electrocardiogram (Fig. 4), however, showed instead the increasing P-R conduction interval known as the "Wenckebach period." This most interesting set of electrocardiograms is reported at this time, not to emphasize or elaborate upon this rare and unusual electrocardiographic evidence of an odd type of block, but to further introduce evidence as to the possible relationship between strains

of a severe type and heart conduction interference. His disability continued, but gradually cleared up. (See electrocardiographic tracings, with their explanation—Fig. 5).

One month after his strain and the development of his difficulty he had apparently returned to normal in terms of his feelings, capacity and heart tones, with a complete disappearance of his dyspnea and signs of passive congestion. The electrocardiogram was then practically normal, with the exception of evidence of slight left ventricular predominance (Fig. 6).

This sequence is in itself interesting, since certain positive findings can be submitted to support the assumption that a sudden lift was followed by incapacity and an objective insult to the heart. His story is further complicated by his statement that seven years previously, after a severe strain in fitting a heavy plumbing connection, he had almost the same type of pain, dyspnea and disability, but of lesser severity and lasting in all about one week.

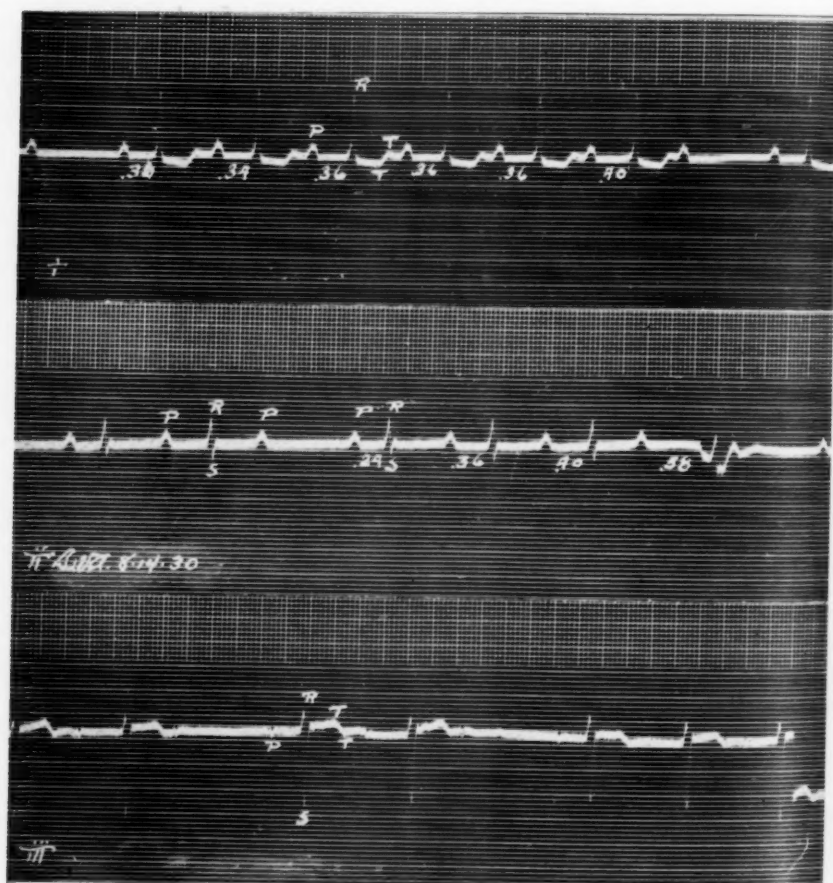


FIG. 4. Record shows an increasing P. R. interval from 0.24 to 0.58 of a second, and resulting in dropped ventricular beats. This "Wenckebach period" indicates a disturbed conduction in the auriculoventricular node, and frequently is the forerunner of complete block.

He offers no neurotic tendencies, and is all too eager to get back to work; he is extremely definite in his statement as to the parallelism which existed between the two spells.

To attempt to identify his pathology is admittedly difficult. Because of his dramatic improvement and the site of the heart block, coronary infarction can be ruled out. As to the auricular fibril-

lation cases no one speaks with much certainty about the circulatory channels in the auricles. Indeed, aside from the epoch making discoveries of Keith and Flack and those of Tawara, little is known about the neuromuscular auricular tracts.

The thesis we have been developing leads up gradually from severe lethal trauma to the heart, through disturb-

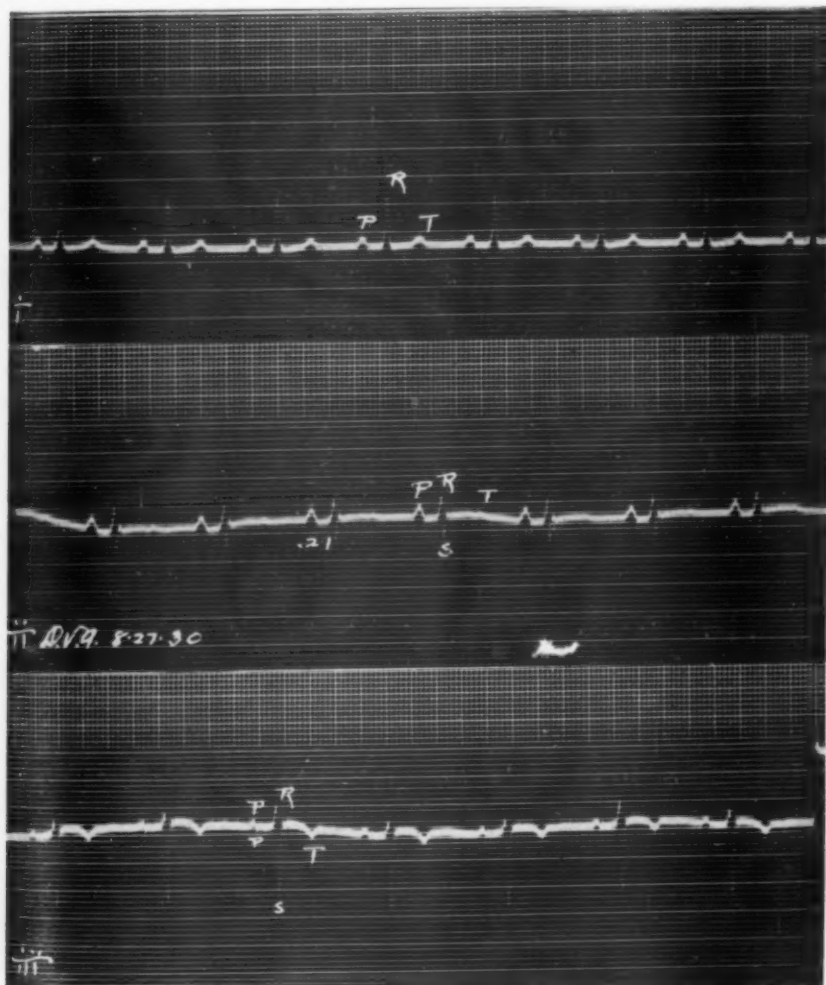


FIG 5. This record shows a definite improvement in the conduction of the auriculoventricular node, and contains a uniform P. R. interval of 0.21 of a second. An improvement is also noted in the T-wave.

ances of function that permit of objective demonstration, to a final word on cardiac instability and subjective incapacity following upon localized chest trauma. We guardedly enter upon a discussion of this group for reasons fully obvious to all those who see many instances of so-called cardiac neuroses or poorly employed by-products of a mass production era. In retrospect, it

occurs to us that in the past we may have paid too little attention to persistent heart symptoms—arrhythmia, actual or near approach to paroxysmal tachycardia—following chest injury. It is well to remember the devastations known to follow cerebral concussion—even without fracture of the skull—where severe shock and memory effacement have obtained.

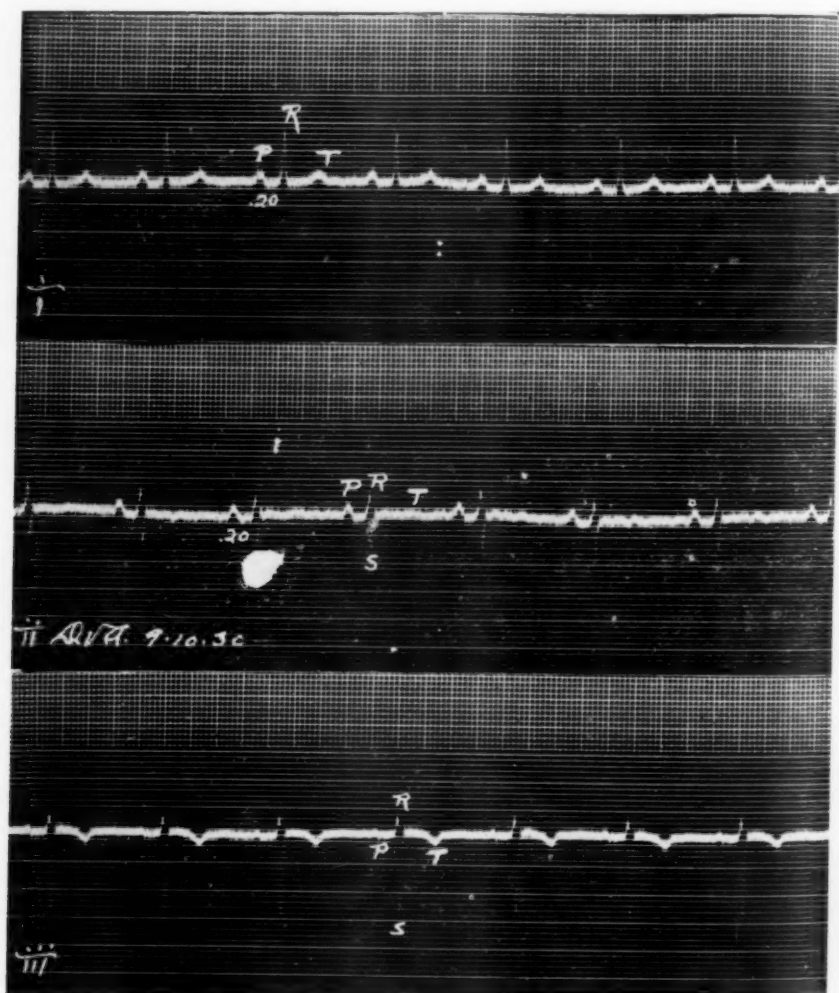


FIG. 6. Record taken two weeks after that shown in Fig. 5 indicates a still greater improvement in the auriculoventricular conduction and there is a uniform P. R. interval of 0.20 of a second.

A vigorous young woodsman, Mr. F. W., aged 19, from the upper Michigan lumber woods, came for examination in August, 1929. About one year previously he had suffered from "a severe strain of his chest when pulling upon some heavy ties," which was his regular sawmill work. These ties were rather heavy, and as they came from the saw it was his job to grasp them and drag them toward himself with a pair of tongs. After a pull in which he partially lost his balance he stated that "something seemed to let go in my chest and throat."

Here we were dealing with a young phlegmatic boy, who had never been conscious of his chest before nor had he lost any time from work. His chest was strapped up, and he complained of more or less discomfort for about three weeks. At recurring intervals for the intervening year he tried to go back to this work, but after a day or two would again experience the same severe, lancinating pains in his chest, and had to give it up. He described these pains as a feeling of tearing within, followed soon thereafter by a sense of suffocation, that greatly annoyed him but did not seem to be accompanied by an appreciable tachycardia.

Our examination involved everything of an objective nature commonly done. Particular evidence was given to the possibility of the various types of diaphragmatic herniation. Nothing whatever objective was found.

An instance comes to mind also of a somewhat older man (35 years), seen first in September, 1929. One year previously he had been the victim of a cave-in in an underground iron mine. He remained thus engulfed for nearly two days, and when removed was naturally very exhausted. Thereafter he gradually recovered, but very little effort continued to bring on distress in his chest, with a tendency to palpitation. At examination objective findings were again total-

ly lacking, including electrocardiographic tracings, outlines of the heart, esophageal and gastric barium visualization, etc. He had sweaty hands and the makeup suggesting the indefinite syndrome of "irritable heart." He was markedly improved under a systematic plan of deep breathing, re-education and graduated exercise.

The lung can also show violent tears from non-penetrating and non-fracturing chest blows. A 12 year old boy after a car accident had a 4 inch laceration deeply into the lower right lobe of his lung, and died of general shock as well as hemothorax. At autopsy his ribs and sternum could be easily pressed down and flattened out against the spinal column without any rib fracture, with full restitution to normal external relation on release. Two boys rode at very high speed into an express train in a fog at a crossing. The one was decapitated; the other (aet. 20) had many body and chest contusions, a fractured right clavicle and multiple left leg fractures. Just as he developed a choking of his optic discs without skull fracture, he developed after extreme shock a shift of his heart markedly to the right, with a drop of his diastolic pressure to zero, with extreme cyanosis, all without rib fracture. The oxygen tent rescued him both from his shock and massive atelectasis accompanying internal pulmonary hemorrhage. For four days he spit up considerable blood, but ultimately recovered.

COMMENT

The subject which we have discussed is a sort of "no man's land" between medicine and surgery. Increasing interest is manifested as indicated in a slowly developing literature. Internists should take an interest in it; sur-

geons are too easily satisfied with attention to bony breaks.

Fatal injuries where postmortems are not sought for and carefully done leave little working knowledge of the gross and minute organ damage. Any group of accidents fails to leave its rightful heritage to medical practice and experience where careful clinical and autopsy examinations have not been made. The non-fatal cases and those saved by promptness and precision teach us not only the rationale of immediate therapy but sources of succeeding morbidity.

It is seen that even apparently minor injuries should not be dismissed too casually. Possibly if our man who died at the movie theatre had had a careful review by an internist alive to the possibilities of non-fracturing or penetrating chest injury, a long rest corresponding to that imposed upon cases with coronary infarction might have tided him

over to safety and some years of comfort.

CONCLUSIONS

1. Youthful resilient thoraces permit extreme compression without fracture.
2. The thoracic viscera, like the abdominal, may be torn and lacerated—early and late heart chamber rupture may result, all without even external bruising.
3. Granting this, it must be possible that non-fatal degrees of laceration and hemorrhage may occur. These, with edema or simple trauma, may induce definite physiological perversions. Auricular fibrillation and degrees of heart block are discussed.
4. The border ground between traumatic or compensation neuroses and actual cardiac distress after chest injury is touched upon.

BIBLIOGRAPHY

- ¹HIRSCHFELDER, A. D.: "Diseases of the Heart and Aorta." Lippincott, 1918.
- ²KUGEL: *Med. Wochenschrift*, Prague, 190. 1909.
- ³TUOHY, E. L., AND BERDEZ, GEORGE: "Two Instances of Perforation of the Heart following non-penetrating Chest Injury." *Minn. Med.*, Vol. 9:144, 1926.
- ⁴KAHN, MORRIS H., AND SAMUEL: "Cardio-vascular Lesions following Injury to the Chest." *Ann. of Int. Med.*, Vol. 2, No. 10, 1013-1047.
- ⁵LEVISON, LOUIS A.: "The Relation of Trauma to Cardiac Disease." *Ann. of Int. Med.*, Vol. 1, No. 4, 227, Oct., 1927.
- ⁶THEIM, C., AND COLLABORATORS: "Handbuch der Unfallheilkunde." Second Ed., Vol. 2, part 2, p. 237.
- ⁷LUBARSCH, O., AND HENKE, F.: "Handbuch der Speziellen Anatomie und Histologie." Zweiter Band, 1924, 470-473.
- ⁸WHITTEN, M. B.: "Review of Technical Methods of Demonstrating Circulation of Heart; Modification of Celluloid and Corrosion Technique." *Arch. of Int. Med.*, 42:846-864, Dec., 1928.
- ⁹WILLIUS, FREDERICK A.: "Clinical Electrocardiography." W. B. Saunders Co., 1922.
- ¹⁰WILLIUS, FREDERICK A.: "Clinical Electrocardiograms." W. B. Saunders Co., 1929.
- ¹¹WHITTEN, M. B.: "The Coronary Circulation as related to Myocardial Infarction." *Proc. Staff Meetings, Mayo Clinic*, pp. 130-132, April 24, 1929.
- ¹²BARNES, A. R., AND WHITTEN, M. B.: "Study of T-wave Negativity in Predominant Ventricular Strain." *Am. Heart Journ.*, 5:14-67, Oct., 1929.
- ¹³BELL, AARON, M. D., AND PARDEE, HAROLD E. B., M. D.: "Coronary Thrombosis." *J.A.M.A.*, 94:1555, May 17, 1930.
- ¹⁴GILCHRIST, A. RAE, AND RITCHIE, W. T.: "The Ventricular Complexes in Myocardial Infarction and Fibrosis." *Quar. Journ. Med.*, London, 91:273, April 1930.

Chronic Meningococcemia Without Localizing Signs*

Report of a Case

By SAMUEL S. RIVEN, M.D., *Nashville, Tenn.*, AND ABEL A. APPLEBAUM, M.D., *Ann Arbor, Mich.*

CHRONIC meningococcemia without localizing signs is a comparatively rare disease, although more frequent reports of its occurrence have appeared in recent years. It offers an explanation for a limited number of cases of prolonged fever without any apparent cause. Gwynn in 1898 first demonstrated the meningococcus in the blood stream. Salomon¹ (1902) described a sepsis which persisted for eight weeks and repeated positive blood cultures for the meningococcus were obtained. A localization of the sepsis in the meninges was noted later. Further instances of meningococcus septicemia have been reported by Andrewes², Liebermeister³, Warfield and Walker⁴, Morgan⁵, Neergard⁶, Graves, Dulaney and Michelson⁷, Spirit and Braun⁸, Lemmers-Danforth⁹, Dock¹⁴, and Vesell and Barsky¹⁰. In all cases diagnosis was made by bacteriological procedures or necropsy.

The source of infection by the meningococcus has been in dispute for some time. Without a doubt the or-

ganisms are first harbored in a focus most commonly located in the nasopharynx. It was thought at first that infection of the meninges took place by direct extension from the nasal mucosa through the ethmoidal cells and cribriform plate of the ethmoid. The infection may spread through lymph channels or more likely the blood vessels. (Herrick¹¹, Elser and Huntoon¹².) Herrick emphasizes that a meningococcemia always precedes involvement of the meninges and is characterized by symptoms of sepsis lasting several hours to several days during which time the organisms may be isolated from the blood stream. The majority of reported cases including the one under discussion here present evidence for the hematogenous route of infection.

Various classifications of meningococcemias have been presented; of these probably the most complete and more recent is that of Graves, Dulaney, and Michelson⁷. They divide meningococcemias into two main groups, the acute and chronic. Acute meningococcemia is that form in which general sepsis is of less than one week's duration prior to localization in some one

*From the Department of Internal Medicine, University of Michigan Hospital, Ann Arbor, Michigan.

organ. This includes the fulminating type with a fatal outcome in from eight to twenty-four hours after the onset, and also the type which is followed by localization in the meninges. Chronic meningococcemia is the form in which the sepsis is present more than one week and terminates in most cases by localization (meningitis, endocarditis) or, in a few instances, by a continuation of the generalized form of the disease.

To date, seventeen cases of chronic meningococcemia have been reported in American medical literature, although a much larger series appears in foreign periodicals. Of these seventeen cases including the one reported here—five showed localization in the meninges with recovery, one had localization in the endocardium and then metastasis to the meninges and death, two localized in the endocardium and terminated fatally. A second group of nine showed no localization, of these eight recovered. The case reported here falls into this infrequent form of chronic meningococcemia without any localization or metastasis.

REPORT OF A CASE

History: A. T., white male, age 44, married, Finnish, a painter and decorator, was admitted to the Medical Service of the University Hospital on July 5, 1930, complaining of pains in the extremities, weakness, and a blotchy skin eruption. His illness dated back to May 19, 1930, when he noticed a chilly feeling, fever, and an aching sensation all over his body which lasted for twenty-four hours. The following day the chilly feeling was gone but the aching continued in the feet, legs, hands, forearms, neck and occiput and was made worse on motion. The patient was forced to give up his occupation because of weakness and difficulty in walking. At no time was there

redness, swelling or heat over the joints. These symptoms were not continuous but would come about once a week associated with fever and mild sweats and would last for two or three days. About June 1, 1930, a little over one week after the onset of his illness, the patient noticed a rash appearing first on the dorsum of his left foot and then in varying degrees on the arms, legs, palms, soles and trunk but none on the face. These lesions, he described as varying in size from pin-head to pea size, were rose colored, elevated, not painful, and underwent involution in the course of one week leaving a brownish hyperpigmentation. The skin lesions appeared in crops accompanying the rise in temperature and generalized symptoms described above. During his illness the patient was constipated, appetite was poor, and he lost about fifteen pounds in body weight in seven weeks prior to admission.

The past history threw no light on the present condition. There were no other people in his community suffering from a similar illness.

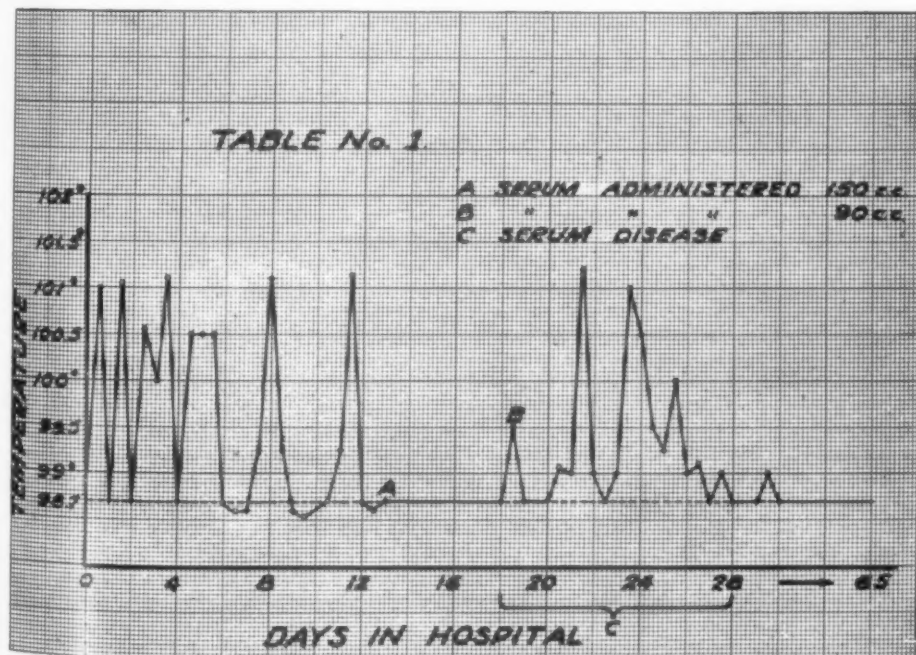
Physical Examination:—The patient was a middle-aged foreign male who appeared fairly well nourished, but ill. There was no apparent pain or discomfort. The skin and mucous membranes showed a distinct pallor. On the extremities and trunk there was a maculo-papular eruption with the lesions undergoing various changes of involution, the color ranging from rose to brownish pigmentation, size varying from pin-head to pea size, deeply seated and only slightly elevated above the surrounding skin. They were fairly firm to palpation, and not tender. The lymph glands, including the cervical, axillary, epitrochlear, and inguinal glands were moderately enlarged, discrete, but not tender. The pupils were equal and reacted to light and accommodation. The fundus examination revealed no abnormalities. The teeth showed caries and there was a definite pyorrhea present. The throat was not reddened and there was no exudate. There was no tenderness over the sinuses, antra or mastoids. There was no stiffness of the neck. Examination of the heart and lungs was negative except for a few crackles at the right apex which disappeared in the course of a few days. Blood pressure was

128/75. The edge of the spleen was just palpable, further examination of the abdomen showed no gross abnormalities. The joints were freely movable both on active and passive motion. Neurologic examination revealed no neck rigidity. The pupils were normal. There was slight weakness of the left side of the face. The biceps, triceps, knee, and Achilles' jerks, and abdominal reflexes were increased in intensity. No Kernig sign, Brudzinski sign, Babinski sign or ankle clonus was present. Considerable tremor on finger to nose test, more on the right side, was present with the eyes both open and closed. There was no evidence of meningeal irritation except the increased intensity of the reflexes which may have been present prior to the patient's present illness; these findings were more compatible with a mild toxemia than any other form of central nervous system involvement.

The tentative diagnoses on admission were undulant fever, typhoid and paratyphoid fever, secondary stage of syphilis with roseola, erythema nodosum and pulmonary tuberculosis.

Course and Treatment:—

The Kahn test of the blood serum for syphilis was negative. Blood culture and agglutination tests for *B. melitensis*, *B. tularensis*, *B. abortus*, *B. typhosus* and paratyphosus taken on August 7, 1930, were reported negative and the blood culture showed no growth on the third day. There was a slight anemia present—hemoglobin 76% (Sahli), red blood cells, 3,700,000 per cu. mm., white blood cells 14,800 per cu. mm. X-ray examination of the chest was negative, showing no evidence of pulmonary tuberculosis. The temperature was intermittent in character with an afternoon rise to 101° F. and fall to normal during the night and morning (see table No. 1). From July 9 to July 11, 1930, the temperature remained elevated to 100.3° F. and associated with this rise there were pains in the arms, legs and occiput, and a feeling of malaise. With this myalgia and arthralgia a maculopapular rash appeared. On July 11, 1930, the temperature fell to normal and the pains and rash disappeared. On July 13 and again on July 16 there was a morning febrile rise



to 101.4° with the same symptoms noted above. During these rises the white blood cell count rose to 20,000 per cu. mm. Blood cultures were taken at the height of the fever. After seven days cultivation of the first blood culture and two days cultivation of the second, both flasks showed a growth of gram-negative diplococci which were agglutinated by polyvalent anti-meningococcus serum.

On the basis of the laboratory findings a diagnosis of meningococcemia without any localization was made. No lumbar puncture was done because of the absence of symptoms of meningeal irritation and the possibility that it might favor localization in the meninges.

On July 18th after routine desensitizing doses of horse serum he was given 60 cc. of polyvalent antimeningococcus serum intravenously. On the following day he received 90 cc. more making a total of 150 cc. of serum. There was no immediate reaction from the serum except for a slight backache which passed off at once. Smears were taken from the nasopharynx which were reported as positive for the meningococcus. Following the first serum administration the temperature promptly dropped to normal for 5 days and all symptoms subsided. On July 23rd there was a slight febrile rise to 99.4° F., recurrence of symptoms was feared and the patient was given 90 cc. of serum intravenously in 3 doses of 30 cc. each. On the seventh day after administration of the first serum the patient developed serum sickness which subsided after treatment with epinephrin and ephedrin. Repeated consecutive

blood cultures taken at intervals varying from four days to two weeks were consistently reported as showing no meningococci. (See table No. 2).

On July 18th swabs were taken from the nasopharynx. Direct smear and culture both showed the presence of meningococci. Saline irrigations of the nose and throat followed by instillations of 25% solution of argyrol were instituted three times a day. Nasal cultures remained positive even in the presence of negative blood cultures until August 17th after which time repeated nasal cultures were negative. After the temperature had subsided the patient was placed on a high caloric diet and in the course of six weeks gained twenty-four pounds in body weight. His general condition improved remarkably and he was discharged as cured on September 7, 1930, one hundred twelve days after the onset of his illness or sixty-five days after admission to the University Hospital.

ADDITIONAL LABORATORY DATA*

The first two blood cultures taken on July 7th and July 16th were positive for the meningococcus. Six succeeding cultures at varying intervals after the administration of polyvalent antimeningococcus serum showed no growth. For five weeks prior to dis-

*Laboratory work in this case was carried out in the University Hospital Bacteriological Laboratories under the direction of Doctor R. L. Kahn and Miss L. D. Henry.

TABLE NO. 2

BLOOD CULTURES		CULTURES OF NASO-PHARYNX	
Date	Result	Date	Result
7- 7-30	meningococci	7-18-30	meningococci
7-16-30	"	8- 1-30	no meningococci
7-18-30	antimeningococcus serum given.	8- 9-30	meningococci
		8-11-30	meningococci
7-18-30	no growth	8-13-30	no meningococci
7-23-30	no growth	8-16-30	no meningococci
7-28-30	no growth	8-19-30	no meningococci
7-28-30	no growth	8-23-30	no meningococci
8- 1-30	no growth	9- 2-30	no meningococci
8- 7-30	no growth		
8-23-30	no growth		

charge he had a negative blood culture. Beef infusion, glucose broth, liver-brain infusion or Hibbler's broth, beef infusion agar and Hibbler's agar poured plates were employed. All media prior to sterilization were titrated to pH of 7.5. The sediment in the flasks of broth and the colonies on the agar plates were examined daily, stained by Gram's method and the type of organism and number of colonies noted. As soon as growth appeared in the sediment a transfer was made to blood agar plates, and from the growth here a bacterial antigen was made and this was agglutinated against the routine diagnostic antisera as well as all obtainable lots of therapeutic antimeningococcus serum. Controls were run in each instance. A correlation of the cultural, morphological, and serological characteristics of the organism found showed it to be a Gram-negative diplococcus which was agglutinated by all available antimeningococcus sera in dilution of 1:320.

Nasal cultures were positive for the meningococcus from July 18 until August 13 after which time they were negative on five consecutive occasions prior to discharge on September 7, 1930.

COMMENT

In view of the increase in the number of reported cases of chronic meningococcemia in recent years, an analysis of the findings seems timely. This is an analysis of the seventeen cases of this disease reported in American medical literature to date.

Duration—The average length of illness was four months, the extremes being from three weeks (Cecil and

Soper¹³, Herrick¹¹) and seven months (Dock¹⁴).

Age—A sepsis of this type may occur at any age period. The youngest patient in this group was twelve years (Marlowe¹⁵) and the oldest forty-four years. Ninety-two per cent of the cases fell into the third and fourth decades of life. The disease apparently is more predominant in males than females (3 to 1).

Clinical Findings—Although there appears to be a characteristic clinical picture of meningococcemia yet a definite diagnosis cannot be made without positive blood culture for the organism. The picture has been ably described by Bloedorn¹⁶, Morgan⁵, and Dock¹⁴. The onset of the illness is usually sudden and is ushered in by a chilly feeling or a definite rigor, headache, malaise, fever and sweats. Following closely upon this are progressively increasing weakness, myalgia and arthralgia, a multiform rash, and an intermittent type of fever. The patient does not appear to be critically ill but has only a mild type of sepsis, with slight generalized glandular enlargement if any, slightly enlarged spleen, pain in the joints and slight limitation of motion because of the pain. The pulse continues to be rapid and often is out of proportion to the temperature.

In the great majority of cases the fever is present from the onset and although usually intermittent in character with rises every day or every other day it may in some instances be septic in type. In thirteen out of seventeen, or 76% of reported cases, the fever was intermittent and in the re-

mainder was septic. The average height of the fever is 101° F. although it rose occasionally to 104° F. The leukocyte count is apt to vary with the fever, ranging from 11,000 to 24,000 per cu. mm.; however, when complicated by a meningitis it may reach 50,000 per cu. mm. or more. The leukocytosis is associated with a distinct rise in the polymorphonuclear ratio to 80% or more. The symptoms present during the febrile rise are not considerable and during afebrile periods the patient may feel perfectly comfortable. The fever may simulate the quartan or tertian types of malaria. Bloedorn¹⁶ reports such an instance in a twenty-one year old patient, who had been ill for one week with headache, drowsiness, and just prior to hospitalization had a chill. Physical examination and all laboratory data for the first week were negative. He had a quartan type of temperature and then a septic course, with rises to 102° F. and 103° F. He developed rose spots, arthralgia, and herpes, and on the eighteenth day positive blood cultures were obtained.

In most cases the arthralgia is not an exceedingly distressing symptom although it is almost always present. It consists of pain in the joints, usually of the extremities and is associated with tenderness over the bones and joints, and limitation of motion due to pain. The joints proper show very little or no destructive involvement, but in a few instances one joint did suppurate. When fluid is present in the joints the meningococcus may be isolated from them.

In all save two instances of the reported cases there was a multiform rash present varying from maculo-

papular, hemorrhagic, purpuric, petechial, erythematous, to those resembling the acute exanthems, *erthyema nodosum*, *erythema multiforme*, rose spots, flea bites, toxic erythemas and even herpes. The lesions are proven to be embolic phenomena resulting from capillary hemorrhages into the skin producing local reactions. Fontanel¹⁷ and LeBourdelle¹⁸ report positive cultures of meningococcus from fragments of the skin taken from a purpuric rash. Brown¹⁹ reports a case of meningococcus meningitis with lesions resembling measles which rapidly changed to large purpuric spots. Microscopic examination showed numerous intracellular and extracellular meningococci. The most common type of rash is maculo-papular occurring in greatest numbers on the extremities and found also on the trunk. The face and mucous membranes are free from the eruption. It is differentiated from *erythema nodosum* by the fact that the lesions are less painful and do not have a bluish border. The rash is usually associated with the arthralgia and occurs in crops with the rises in temperature, undergoing involution between febrile rises. The eruption may be extensive and in few instances may appear with the subsidence of the fever.

Except for the headache and slightly exaggerated reflexes, which may well be present in any sepsis, there are usually no symptoms referable to the central nervous system in this condition unless complicated by localization in the meninges. Lumbar puncture should not be done unless definite signs of meningeal irritation are present because of the danger of predisposing the meninges to infection. However, in the

presence of earliest signs of meningeal involvement lumbar puncture and intrathecal therapy should be instituted at once. In the case reported here no lumbar puncture was done.

Chronic meningococcemia may resemble other infections—most commonly malaria, rheumatic fever, subacute bacterial endocarditis, tuberculosis, undulant fever, typhoid fever, and secondary stage of syphilis. Differentiation is through laboratory procedures.

The most striking feature of this disease is the consistently positive blood culture; in all instances the organisms were isolated from the blood during the clinical course of the disease or at necropsy. During any phase of the disease, positive blood cultures may be obtained, but the organisms grow more rapidly from blood drawn at the height of the febrile rise than during afebrile periods as was demonstrated in this patient. It is frequently desirable to locate the focus of infection and since the naso-pharynx is the most common focus for this organism cultures from the naso-pharynx should be made. Smears and cultures from the naso-pharynx of our patient were positive, and remained so for some time after the blood cultures were negative, finally yielding to therapy directed at this site.

Localization and Prognosis:—In a large percentage of cases localization has occurred in the meninges and heart although it has been reported to have occurred in the joints and nasal accessory sinuses. Eight of the seventeen reported cases of chronic meningococcemia showed localization. Five of

these developed meningitis, two of which terminated fatally; two developed a septic endocarditis, and one a septic endocarditis and meningitis combined, all ending in death. The prognosis in meningococcemia is altered by the associated complications. Analysis of the literature reveals that the prognosis in meningococcemia, uncomplicated, is good, death occurring in but 10% of the patients. Involvement of the endocardium makes the outlook very grave as all patients with this complication have succumbed. When complicated by meningitis fifty per cent in this series died.

Treatment:—A great deal of controversy seems to exist in regard to the efficacy of specific serum therapy in the treatment of meningococcemia. Some authors have reported that the course of the disease was little affected by the use of serum, and a great many other measures such as foreign protein shock, fixation abscesses, autogenous vaccines, and others have been used but with even less striking results. In the cases of Marlowe¹⁵ and the one here reported there was complete subsidence of all symptoms and a disappearance of the organisms from the blood as evidenced by repeated negative blood cultures. In both instances the serum used was found to agglutinate the organisms isolated from the blood. In our case the agglutination titer of the various commercial sera available was tested against the strain of meningococcus isolated and all sera showed the same titer—1 to 320. Serum sickness frequently occurs after the administration of serum.

SUMMARY

1. A case of chronic meningococcemia without localization and followed by recovery is here reported.

2. This is a relatively rare condition but has been more frequently recognized in the last few years.

3. A definite diagnosis of meningococcemia can only be made by positive blood cultures for the organism.

4. The prognosis is very good when no localization occurs.

5. In our case there was complete subsidence of symptoms and consistently negative blood cultures following the intravenous use of specific antimeningococcus serum.

6. Meningococcemia offers an explanation for a limited number of cases of prolonged fever of obscure etiology.

BIBLIOGRAPHY

- ¹SALOMON, H.: Ueber Meningokokkenseptikämie, Berl. klin. Wochnschr., 39:1045-1048, 1902.
- ²ANDREWES, F. W.: A case of Acute Meningococcal Septicemia, Lancet, Lond., 1:1172, 1906.
- ³LIEBERMEISTER, G.: Ueber Meningokokkensepsis, München med. Wochnschr., 55: 1978-1980, 1908.
- ⁴WARFIELD, L. M., WALKER, J. K.: Ulcerative Endocarditis Caused by Meningococcus, Pennsylvania Hospital, Ayer Clin. Lab., 1:81, 1903.
- ⁵MORGAN, H. J.: Chronic Meningococcus Septicemia, Bull. Johns Hopkins Hosp., Aug., 1921.
- ⁶NEERGARD, A. E.: Meningococcus Bacteremia, M. Clin. N. America, 9:461-469, Sept., 1925.
- ⁷GRAVES, W. R., DULANEY, A. D., AND MICHELSON, I. D.: Chronic Meningococcemia; Report of a Case, J.A.M.A. 92:1923-1925, June 8, 1929.
- ⁸SPIRIT, J. AND BRAUN, M.: Zur Klinik der Meningokokkensepsis, Klin. Wochnschr., 6:1048, May 28, 1927.
- ⁹LEMMERS-DANFORTH, I.: Meningococcus Infection Without Meningitis, Ztschr. f. Kinderh., 44:551-555, 1927.
- ¹⁰VESELL, HARRY, AND BARSKY, JOSEPH: Chronic Meningococcus Septicemia, Amer. J. Med. Sc., 179:589-599, May, 1930.
- ¹¹HERRICK, W. W.: Extrameningeal Meningococcus Infections, Arch. Int. Med. 23:409, April, 1919.
- ¹²ELSER, W. J., AND HUNTOON, F. M.: Studies on Meningitis, J. Med. Res. 20:371, June, 1909.
- ¹³CECIL, R. L., AND SOPER, W. B.: Meningococcus Endocarditis with Septicemia, Arch. Int. Med. 8:1, April, 1911.
- ¹⁴DOCK, W.: Intermittent Fever of Seven Months' Duration due to Meningococcemia, J.A.M.A. 83:31-33, July 5, 1924.
- ¹⁵MARLOWE, F. W., JR.: Meningococcemia, Report of Case with Recovery, J.A.M.A. 92:619-621, Feb. 23, 1929.
- ¹⁶BLOEDORN, W. A.: Meningococcus Septicemia, Amer. J. Med. Sc. 162:881, Dec. 1921.
- ¹⁷FONTANEL, P., AND LEBOURDELLES, B.: Diagnosis of Meningococcus Meningitis, Compt. rend. Soc. de biol. 90:766-767, March 28, 1924.
- ¹⁸LEBOURDELLES, B.: Frequent Presence of Meningococcus in Purpura Infections, Presse Med. 33:660-661, May 20, 1925; Abstr. J.A.M.A. 85:154, July 11, 1925.
- ¹⁹BROWN, C. L.: Skin Lesions in Meningococcus Septicemia, Am. J. Dis. Child. 27:598-602, June, 1924.

We are greatly indebted to Doctors Raphael Isaacs and Cyrus C. Sturgis for their valuable aid and suggestions.

Non-Tuberculous Spontaneous Pneumothorax*

With Report of Cases

RALPH L. FISHER, A.B., M.D., *Detroit*

SPONTANEOUS pneumothorax, while occurring fairly frequently in tuberculosis, is a comparatively rare incident in other diseases. As a matter of fact, such authorities as Behier and Jaccoud claim that tuberculosis accounts for ninety per cent of the cases and there are some who even claim that all cases are due to a previous infection with the Koch bacillus. Browder¹ has reported a case with a ruptured sub-pleural abscess as the etiological factor. Lewald² has reported ten non-tuberculous cases with recovery of seven. Idiopathic cases have been observed by Kahn³, Weber⁴, Kelly⁵, Bedford and Joules⁶. Asthma as an etiological factor has been observed by Benedict⁷ and by Emerson and Beeler⁸. A series of twenty-two cases of non-tuberculous origin occurring at the Mayo Clinic has been reported by Lemon and Barnes⁹. Stoll¹⁰ has recorded a series of cases occurring in infants and children as a complication of the following conditions: emphysema, apoplexy, gangrene of lung, pneumonia, pertussis, diphtheria, bronchiectasis, foreign body in lung, infarct, abscess of lung, typhoid and rupture of sub-pleural abscess.

Watson and Robertson¹¹ have reviewed two hundred cases of non-tuberculous spontaneous pneumothorax with a report of three cases. These three cases presented several interesting features. In one case during a five year period the patient had first a collapse of one and then of the other lung. Another case experienced two collapses eight months apart. A third case had fourteen collapses on the two sides and once a bilateral collapse. Physical and X-ray examinations revealed no organic pathology in any of these cases or in three other cases of spontaneous pneumothorax observed by these authors.

CASE NO. I—B. G., white man, age 39, married, a laborer, entered the hospital complaining of severe pain in the chest. The family history is unimportant. The past history revealed that the patient had been subject to asthmatic attacks over a number of years and during the interval between attacks had had a slight cough. There was no history of recent loss of weight, hemoptysis, or night sweats. For the preceding six months he had tired very easily and experienced a slight shortness of breath upon exertion. Just previous to the onset of the present illness he had been suffering from a severe asthmatic attack. Four days previous to admission to the hospital just after going upstairs he suddenly experienced a severe pain in his right chest, had great difficulty in getting his breath and became very cyanotic. The pain and dyspnea had continued

*From the Department of Medicine, Jefferson Clinic and Diagnostic Hospital.

until time of admission, though not quite so severe.

Physical examination showed the patient to be a middle aged man who appeared quite ill and had a rather anxious pinched expression to his face. Temperature was 97.8, respirations 35, and pulse 120. Blood pressure was 112 systolic and 80 diastolic. There was marked dyspnea. Mucous membranes

were pale and skin was loose. He was very undernourished. Pupils were equal and reacted to light and accommodation. Extraocular movements were normal. Eye grounds showed no abnormalities. Examination of the sinuses revealed a chronic purulent ethmoiditis. Tonsils were fairly large and pus could be expressed from the crypts. There was marked pyorrhea of the teeth. Thyroid

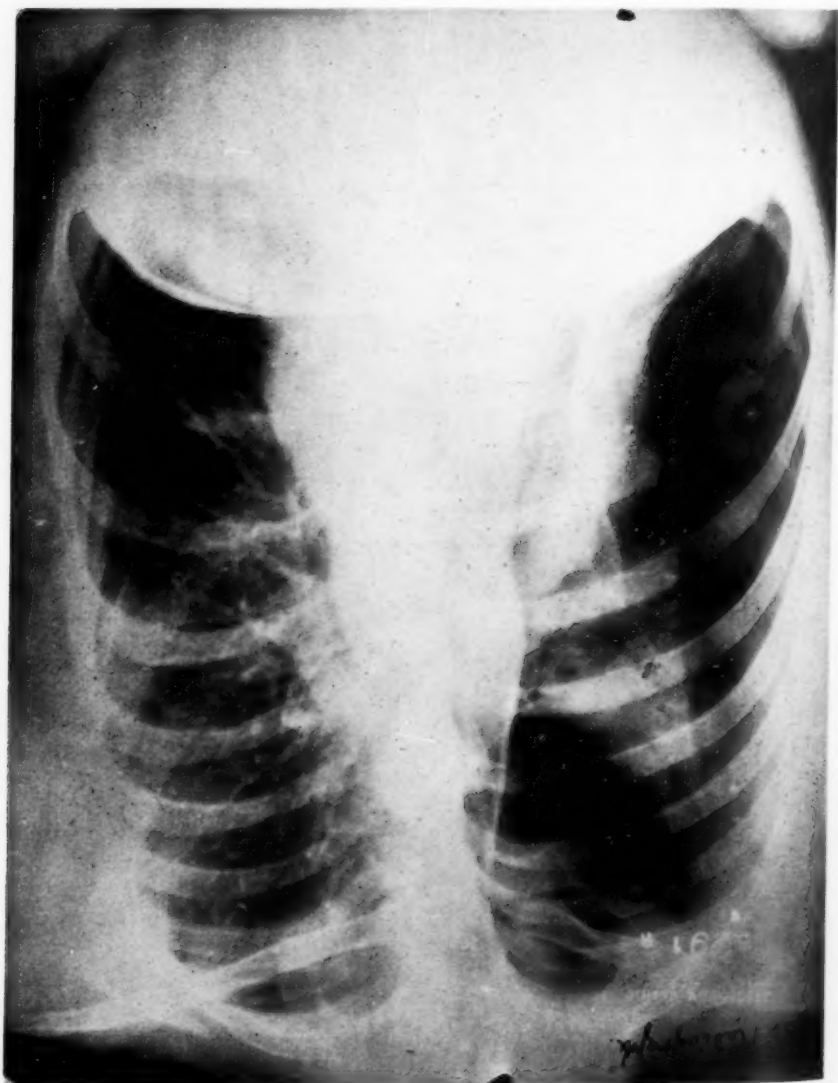


FIG. 1. Radiograph of Case No. I at time of pneumothorax.

was negative. The chest examination revealed that the intercostal spaces on the right side were almost completely obliterated. Vocal fremitus and breath sounds were absent over the right chest. Breath sounds were accentuated over the left chest and many moist râles were heard at the left base. Cardiac dullness extended $11\frac{1}{2}$ centimeters to the left of the midsternal line. The right border could not be made out. Pulse was very rapid, of rather poor quality, but regular. The liver border could be felt one finger breadth below the costal margin. Otherwise

physical examination was negative. Laboratory data showed a normal urine, a mild secondary anemia and negative Wassermann and Kahn reactions. X-ray revealed complete collapse of right lung.

This patient remained in the hospital a little over a month. His clinical condition gradually improved and he was discharged. About eight days after his return home he suddenly became very ill, was markedly dyspneic and cyanotic, and died within a short time.

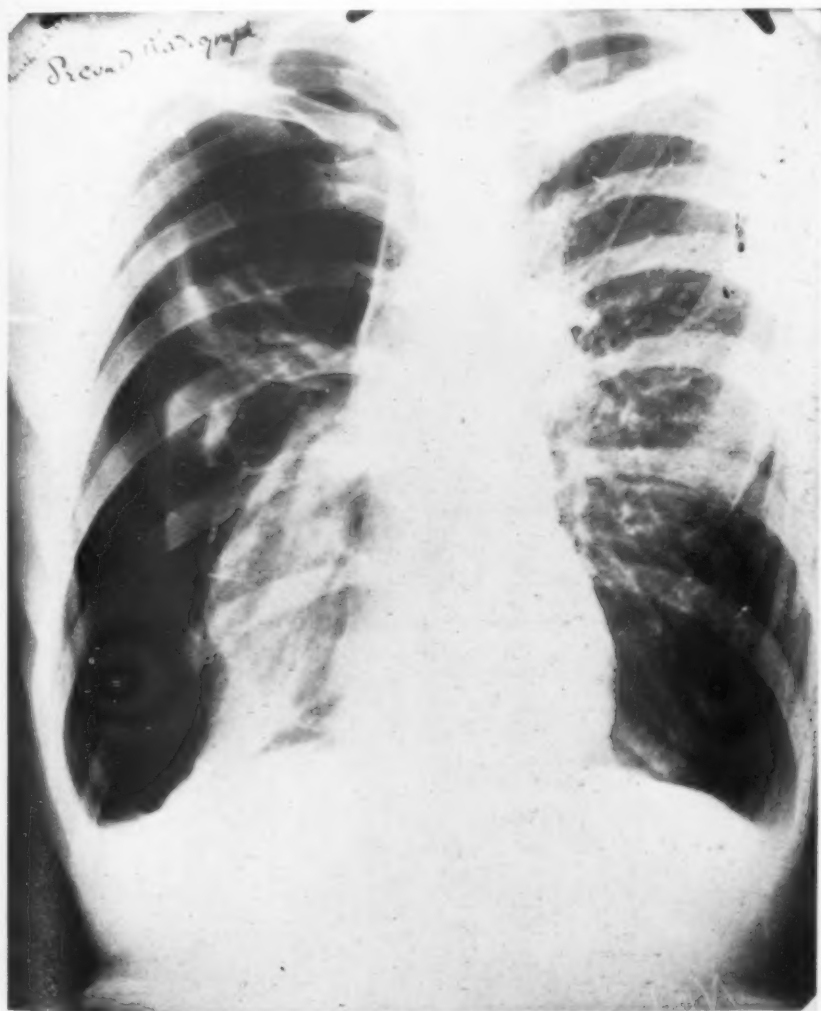


FIG. 2. Radiograph of Case No. I three weeks after pneumothorax.

CASE No. II—This case was that of a young man, 29 years of age, single, and a physician by occupation. Family history negative. Past history revealed that he had frequent attacks of follicular tonsillitis when a student in college. There was a history of chronic otitis media on the right side and mumps and chicken pox when a child. Of temperate habits. No history of cough, night sweats or hemoptysis. Three months previ-

ous to present illness had an operation for acute mastoiditis on right side. Recovery was very slow, patient losing his hearing for three months. Was in a very run-down condition. One afternoon while walking down the street he felt a severe pain in his left chest and collapsed on the sidewalk. Respirations were very labored and pulse very fast, these conditions continuing until time of admission to the clinic.

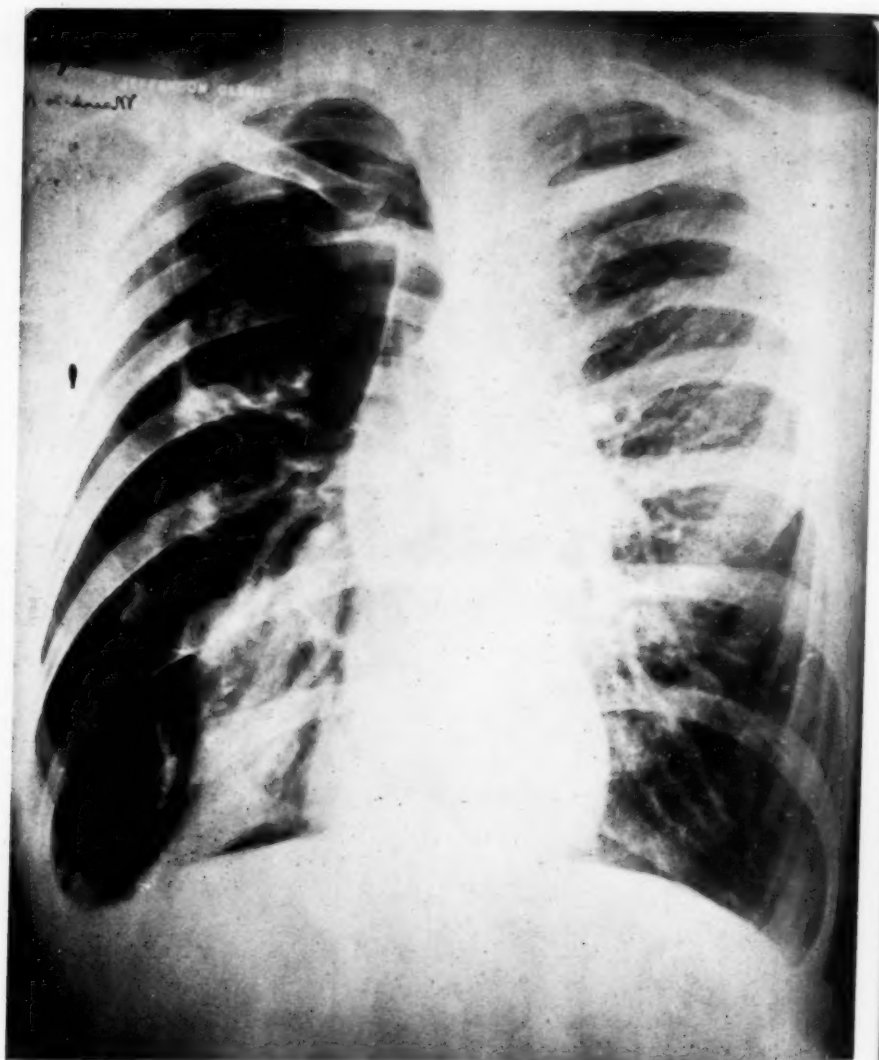


FIG. 3. Radiograph of Case No. I four weeks after pneumothorax.

Physical examination revealed a young man, pale, undernourished, very ill in appearance, and breathing with great difficulty. Temperature 98.2, pulse 130 and respirations 40. The other main positive physical findings were as follows: Coughing was frequent, motion in left chest very limited and intercostal spaces obliterated; absence of voice sounds and vocal fremitus on the left and no audible breath sounds; heart displaced to the right and pulse very rapid with occasional extrasystoles. Laboratory data were unimportant except for moderate secondary anemia. X-ray examination confirmed clinical diagnosis of pneumothorax of the left chest.

This patient very slowly improved, some respiratory embarrassment continuing for several years. It has now been seven years since his illness, and he is in perfect health. A recent X-ray examination revealed no pathology in lung.

CASE No. III (13) is that of a young man 30 years of age, occupation, clerk. Family and past history negative. Five days previous to onset of present illness patient, after cranking his car, experienced pain in his right shoulder. This pain was not very severe and continued until five days later, when out of doors he became cold and started to cough. At this time he felt a flutter-

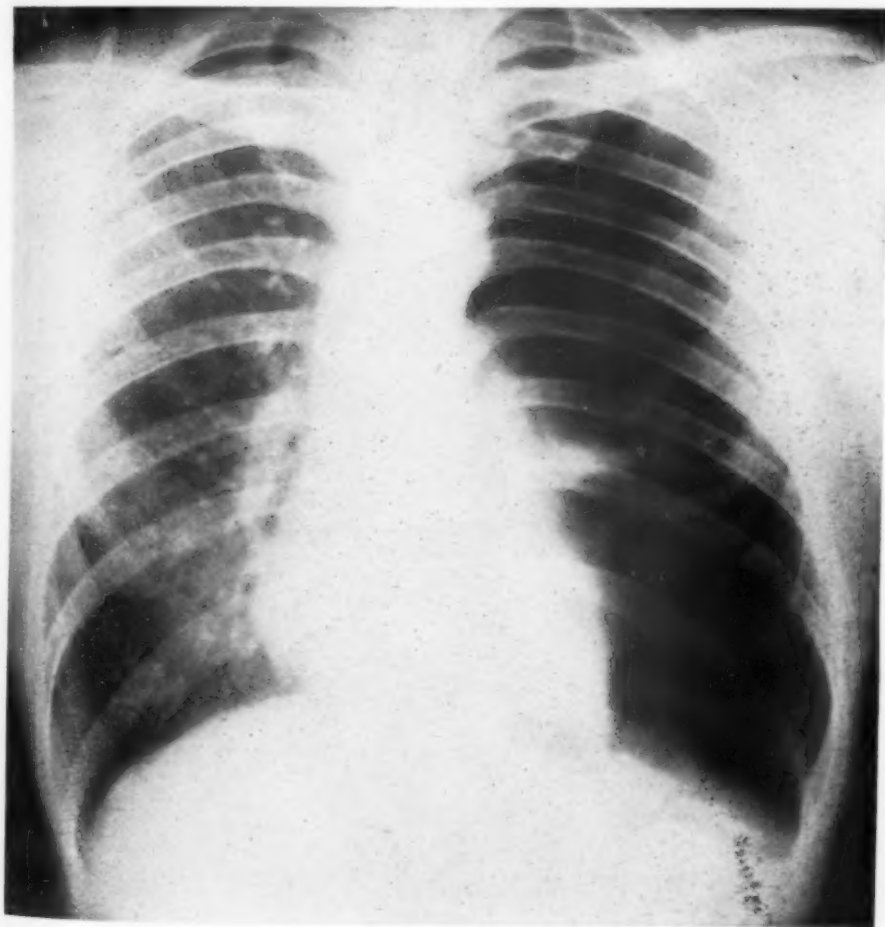


FIG 4. Radiograph of Case No. II at time of pneumothorax.

ing sensation in his throat. He went to bed and remained there for several days. Two days later the cough re-appeared and it was very difficult to stop it. Breath became quite short at th's time also. He remained in bed for a week during which time the cough and pain in shoulder persisted. Recovery was slow and uneventful over a period of three weeks.

Physical examination showed a fairly well nourished young man, coughing frequently and complaining of pain in the region of the right shoulder. Temperature was normal, pulse 100 but of good quality. Respiration was a little labored. Mucous membranes were pale. There was a slight enlargement of the cervical lymph nodes. The right chest showed a limitation of motion and obliteration

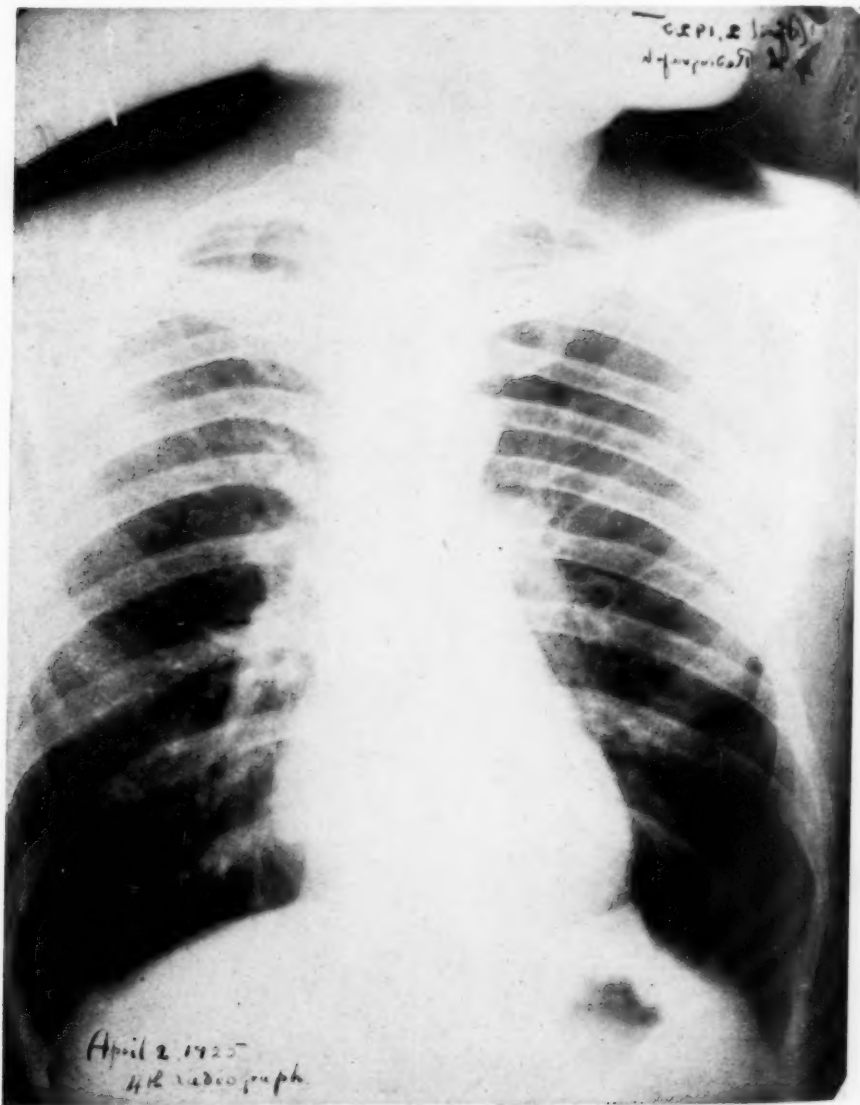


FIG. 5. Radiograph of Case No. II two years after pneumothorax.

tion of intercostal spaces. Voice sounds, breath sounds and vocal fremitus were absent over the right chest. Physical examination otherwise was negative. X-ray showed pneumothorax of right side.

Physical examination of this patient three years later, other than a slight enlargement of the cervical lymph nodes and chronically

infected tonsils, is negative. He has no symptoms of any respiratory trouble at present and is enjoying good health. X-ray examination at present date is negative.

Pneumothorax is a condition that is always secondary to a lesion of the lung or the structure with which it is

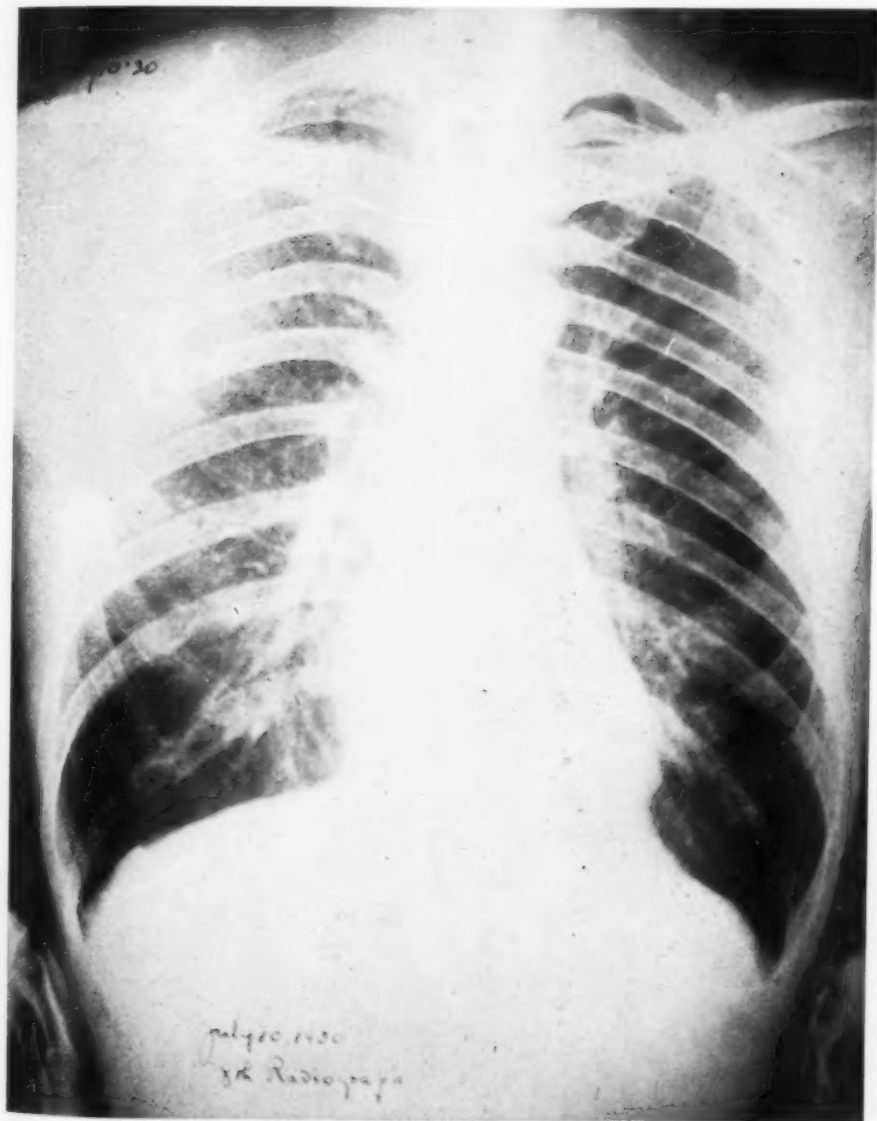


FIG. 6. Radiograph of Case No. II seven years after pneumothorax.

enveloped. According to the Hippocratic writings it was called empyema and it was not until 1759 that Meckel first recognized its significance insofar as respiration was concerned. Its name was given to it in 1803 by Itard and in 1819 Laennec described a simple pneumothorax, pneumothorax with effusion and fistula. Pneumothorax means gas in the pleural cavity. This gas may be hydrogen due

to the action of certain bacteria; to nitrogen used as a therapeutic measure to collapse the lung; or air which enters the pleural cavity as a result of its exposure to the atmosphere. By spontaneous pneumothorax is meant that type which occurs without any demonstrable provocative cause and naturally excludes those cases due to artificial means such as direct trauma and ulcerative communication between

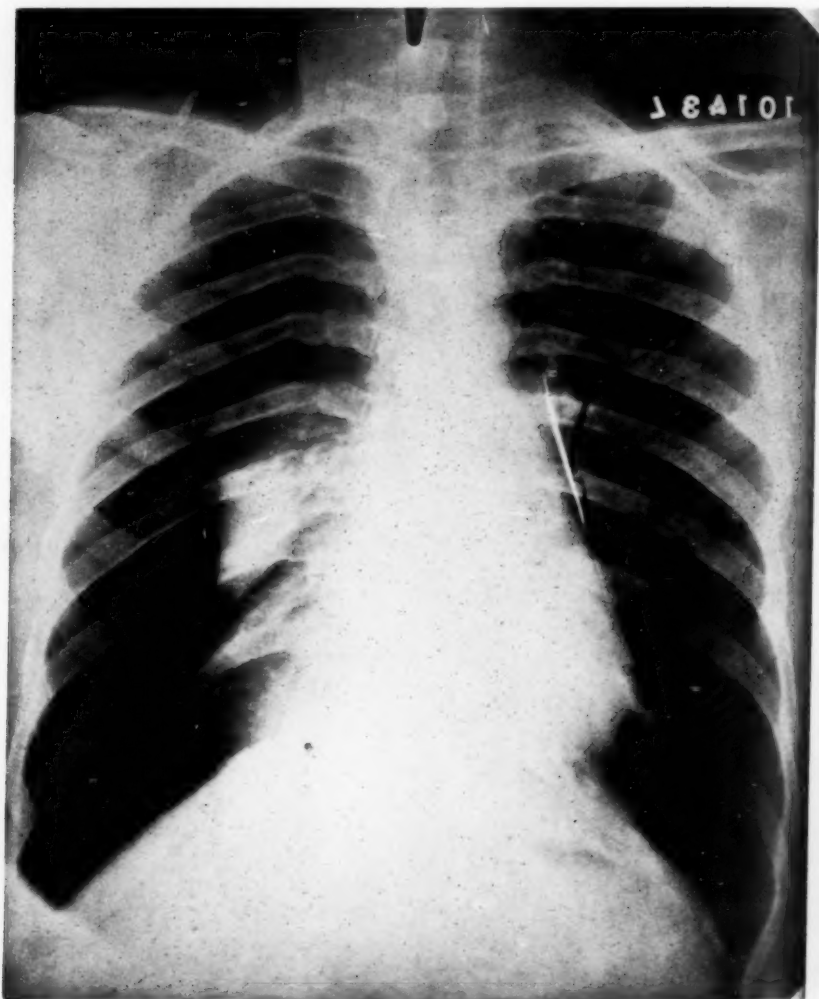


FIG. 7. Radiograph of case No. III at time of pneumothorax.

the alimentary tract and pleural spaces. According to Hegner¹² the most common lesions in the tuberculous type are early small caseating tubercles just beneath the parietal pleura, small superficial tuberculous cavities and interstitial marginal or superficial emphysematous blebs not protected by pleuritic adhesions. So that "any sudden even slight increase in the intrapulmonary pressure or a slight uneven alteration of the pleural tension may cause rupture of the pleura and an

escape of air into the pleural space". Those cases due to asthma probably occur as a result of a rupture of an emphysematous bleb. Even normal lung tissue may rupture when subjected to great strain as occasionally happens in a paroxysm of whooping cough or during parturition.

According to the researches of Wint-rich and Weill, pneumothorax may be of three types: I, the valvular type; II, the open type; and III, closed pneumothorax¹⁴. The valvular type is the one



FIG. 8. Radiograph of case No. III two years after pneumothorax.

usually encountered in spontaneous pneumothorax, the tissues in the vicinity of the tear in the pleura acting as a valve. Air then may enter the pleural cavity easily but is prevented from returning into the bronchial system. And air will continue to pass from the lungs into the pleural cavity until the intrapleural pressure equals that of the intrapulmonic. Thus during inspiration the intrapleural pressure becomes atmospheric pressure whereas during expiration the thoracic cavity collapses, the intrapleural pressure on the affected side exceeds the intrapulmonic, the mediastinum bulges toward the sound side, and the diaphragm on the affected side is depressed. The degree of dyspnea resulting from the collapse of the lungs depends on the functioning ability of the sound lung. It has been shown experimentally that an animal at rest can breathe with but one-tenth of its lung surface functioning without experiencing dyspnea. The sudden pain which usually ushers in the pneumothorax is due to the laceration of the pleura. Similarly the cough is due to pleural irritation and is usually unproductive. The extent of collapse of the lung depends upon the presence or absence of adhesions.

The symptoms of pneumothorax are more or less uniform. It is usually ushered in with acute stabbing pain, sometimes diffuse and sometimes localized, and at times radiating toward the abdomen or spine. As a rule, severe dyspnea accompanies the pain and the patient assumes a sitting posture. He appears anxious, there is cyanosis of the lips and he is covered with perspiration. At first cough is absent and

expectoration is tardy. The pulse is faint and about 120 a minute. The extremities are cold and the temperature may range from 102.2 to 104. Death may occur in several hours, depending upon the functioning ability of the other lung. The dyspnea and other signs of shock gradually disappear, though they may persist for as long as two weeks in the invalid.

The physical signs are characteristic. The affected side is almost immobile, the intercostal spaces are filled and are permanently dilated. Vocal fremitus is abolished on the affected side. Percussion reveals an increase in resonance which may be tympanitic or even amphoric. Auscultation reveals a complete absence of vesicular sounds. There is so-called respiratory silence. Such physical signs as the metallic tinkle of Laennec and the coin sound of Trousseau may be present.

The X-ray findings are exceedingly important. They show in general an enlargement of the hemithorax "with excessive clearness of the pulmonary field so that the shadows of the ribs and intercostal spaces are hardly distinguishable". The collapsed lung may be seen back against the vertebral column and casting a gray shadow. The diaphragm is either lowered or flattened and practically immobile. The mediastinum may be attracted toward the pneumothorax during inspiration.

Insofar as prognosis is concerned, there are two clinical types: I, the rapidly fatal, and II, the non-fatal. In the former death usually occurs within a few hours, whereas in the latter a course of gradual improvement ensues, the air absorbing within five or

six weeks. Recovery may occur in twelve or fifteen days. The outcome also depends upon whether or not there are any complications such as hydro-pneumothorax, pyopneumothorax, etc. It has been estimated that 75% of the cases eventually are fatal.

Treatment should be divided into two heads: I, immediate; and II, during the course of the condition. Immediate treatment consists mainly in relieving the pain with opiates, allaying the cough, and general constitutional measures for the shock. If it is of the suffocating type, decompression of the lung, mediastinum and heart may be necessary. If the pneumothorax remains, fluid is quite apt to develop; in this case withdrawal of the fluid if it becomes abundant and injections of nitrogen are measures to be followed. In case the fluid becomes pus, it may be even necessary to do a

thoracotomy. Later, blowing into bottles may help re-expand the lung.

SUMMARY

(1) A hasty review of the literature is given.

(2) Spontaneous pneumothorax is reported in one case with asthma as causative agent. In a second case no cause was apparent. In a third case physical exertion seems to have had an etiological bearing upon its occurrence.

(3) Symptomatology, physical signs and treatment of pneumothorax are discussed.

(4) The impression is gained that idiopathic spontaneous pneumothorax is of much more frequent occurrence than is generally recognized.

(5) These cases give further support to the contention that spontaneous pneumothorax is not necessarily secondary to infection with tuberculosis.

BIBLIOGRAPHY

¹BROWDER, JEFFERSON: Case of Spontaneous Non-tuberculous Pneumothorax from Ruptured Subpleural Abscess, *American Journal of Surgery*, 8: 415, 1929.

²LEWALD, L. T.: Bilateral and Unilateral Non-tuberculous Spontaneous Pneumothorax, *Archives of Surgery*, 12: 440, 1926.

³KAHN, I. S.: Idiopathic Spontaneous Pneumothorax, Apparently Non-tuberculous, *J.A.M.A.*, 84: 1061, April, 1923.

⁴WEBER, F. P.: Some Unusual Cases of Spontaneous Pneumothorax, *The Practitioner*, 102: 190, April, 1919.

⁵KELLY, F. H.: A Case of Spontaneous Pneumothorax, *Lancet*, 209: 496, 1925.

⁶BEDFORD, DR. EVANS & JOULES, H.: Case of Bilateral Spontaneous Pneumothorax, *British Medical Journal*, 2: 240, 1929.

⁷BENEDICT, C. C.: Pneumothorax Spontaneous Bilateral with Report of Three Cases. *U. S. Veterans' Bureau Medical Journal*, 4: 599, July, 1928.

⁸EMERSON, CHAS. P. & BEELER, RAYMOND C.: An Unusual Case of Double Spontaneous Pneumothorax, *American Journal of Roentgenology*, 10: 126, 1923.

⁹LEMON, WILLIS S. & BARNES, A. L.: A Clinical Study of Fifty Cases of Pneumothorax, *The Journal of the Iowa State Medical Society*, 12: 81, 1922.

¹⁰STOLOFF, E. GORDON: Spontaneous Non-tuberculous Pneumothorax in Infancy and Childhood, *American Journal of Medical Sciences* 176: 657, Nov., 1928.

¹¹WATSON, EVERETT E. & ROBERTSON, CHURCHILL: Recurrent Spontaneous Pneumothorax, *Archives of Surgery*, 16: 431-38, 1928.

¹²HEGNER, C. F.: Accidental Pneumothorax, *American Review of Tuberculosis*, 14: 586, July-Dec., 1926.

¹³Case reported through courtesy of Dr. O. O. Fisher.

¹⁴SERGEANT, E. & COURCOUX, A.: General Pneumothorax. *Nelson's Loose Leaf Living Medicine*. 3: 558.

Cardiac Overaction

The Most Constant and Most Dependable Sign in Thyroid Toxicity*

By HENRY J. VANDEN BERG, M.D., F.A.C.S., *Grand Rapids, Michigan*

THE heart seems to be the first organ to show definitely the effects of thyroid toxicity. With this statement everyone seems to agree. This toxicity is manifested early in the heart action in that the rate is accelerated and the force of the beat is increased. Acceleration of the heart rate is one of the most common physical signs one meets in clinical medicine, whereas cardiac overaction occurs in comparatively few conditions. It may be presumed that all organs and tissues are affected by thyroid toxicity, but none can be so advantageously measured and studied as the heart, both because of its position and because it is constantly in action. No other organ likewise affected will so early produce definite symptoms directed to itself.

Since thyroid toxicity does manifest itself so early in misbehavior of the heart, it naturally follows that the detection of any alteration from the normal in heart action is very important.

In my experience, cardiac overaction in thyroid toxicity is a more constant sign than rate acceleration. It is, in fact, the most constant single sign in goiter toxicity, and it is one of the

earliest. Because of this, its importance should be emphasized, but it is not. The sign, when referred to in the literature, is mentioned, as a rule, in the most casual way. It oftentimes is not mentioned at all.

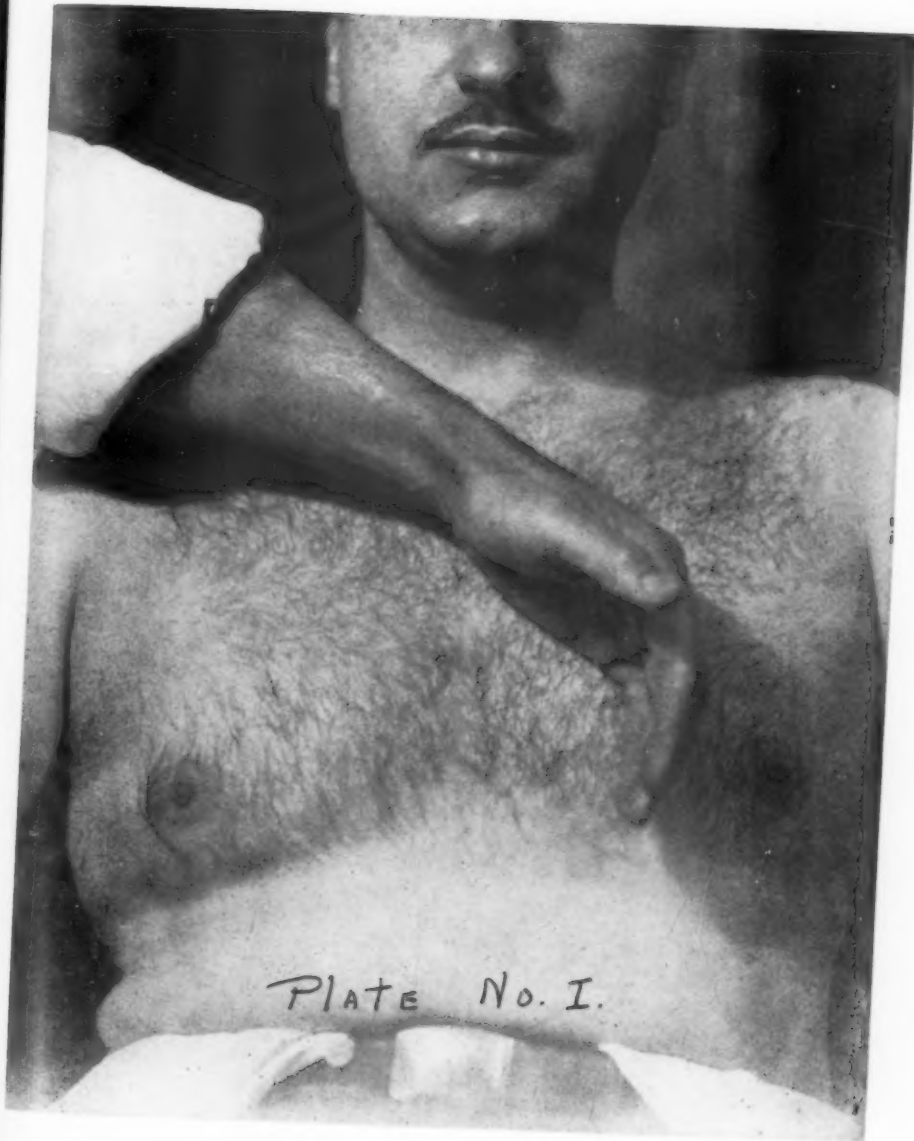
Cardiac overaction is to be elicited by (a) palpitation, and (b) auscultation.

PALPATION

In palpation the technique is important if any one is to get the greatest possible assistance from its use.* The inner aspect of the hand should be used (see Fig. 1), not the palm, and it is obvious that a light hand should be practiced. In thyroid toxicity both the right and left heart are in a state of overaction; consequently the increased impulse will be present over the entire precordial area and usually for a variable distance beyond. The distance beyond will depend upon the intensity of the overaction and it naturally will be altered in the presence of a thick, heavy wall and more so if emphysema is also present. The impulse is a quick, sharp slap or thrust. It is quite different from that in overaction that occurs in hypertension. In

*From the Grand Rapids Clinic.

*For this technique I am indebted to one of my teachers, Prof. Kovacs of Vienna.



the latter the impulse to the palpating hand is comparatively long, slow and heaving, and it is confined, in a well compensated case, to the left heart. Overaction of the hypertension type is best elicited by using the tips of the fingers.

AUSCULTATION

There is a normal intensity relation between the first and second heart sounds with which one should be perfectly familiar if he is to detect slight variations from the normal. The normal first sound is long, more or less loud, and low pitched; the second sound is shorter, less loud and higher pitched. Under thyroid toxicity the character of the heart sounds changes. The first sound becomes shorter, louder and higher pitched; rather soon the pitch becomes as high or higher than that of the second sound. The degree of variation from the normal is dependent upon the degree of toxicity and perhaps somewhat upon the length of time of toxicity. For the purpose of convenience, and of one's records, cardiac overaction can be divided into four grades—for example, overaction grade I, overaction grade II, and so on. In a goiter, then, that is definitely toxic, one will be impressed by the first sound being quick, short, loud and snapping.

It is interesting to note the change in the intensity of the heart action during the pre-operative management. It calms down materially in nearly every instance, quite in keeping with the general improvement. It is furthermore interesting to note the change that follows surgery. In some cases the character approaches the normal almost immediately—in a day or two; in

others it will be a matter of a week or weeks, or even a few months. Cases in which a slight degree of overaction persists are those which are still somewhat toxic. *This overaction is the best clinical criterion or measure to go by to determine the presence of remaining toxicity.* Palpation, of course, goes hand in hand with auscultation.

Cardiac overaction of the thyroid type does occur in conditions other than in toxic goiters. They are (1) excitement (temporary); (2) mitral stenosis; (3) anemias; (4) fevers.

EXCITEMENT, (temporary)

The nervous, supersensitive type of individual will often have, especially when first seen, acceleration of the pulse rate, an increase in the force of the heart beat (thyroid, in type), and other signs that resemble those seen in mild thyroid toxicity. Since a very considerable percentage of patients are of this constitution, the question of differentiation between a simple supersensitive reaction and a superimposed mild thyroid toxicity confronts one almost daily. If, after leaving such a patient to rest for half an hour or so, the heart does not quiet down, the question of a thyroid factor demands further observation and study (metabolism determination, and so forth).

MITRAL STENOSIS

Upon both palpation and auscultation the well compensated heart of mitral stenosis may resemble very closely the behavior of a toxic goiter heart. There are, however, distinguishing points that make it possible to make the differentiation. A thrill may be present in both, but much more fre-

quently in mitral stenosis. The most helpful point of differentiation is the timing of the thrill which may, of course, become difficult in a very rapid heart. The presence of a thrill is best made out with the palm of the hand. Murmurs, if present, are likewise differently timed, systolic in the case of pure hyperthyroidism and, of course, diastolic in mitral stenosis. Secondary signs such as an accentuated second pulmonic sound, the usual small pulse in a well compensated case of mitral stenosis, and the large pulse pressure in cases of hyperthyroidism, afford evidence that is helpful in arriving at a diagnosis. It must always be borne in mind that the two conditions may be simultaneously present. If a suspected thyroid factor in the case of mitral stenosis cannot be finally eliminated, the patient should be given the benefit of the doubt and accordingly should be advised to have the thyroid removed, since it can be done with a great degree of safety. The same principle and reasoning should obtain in all cardiac cases in which the question arises, and more especially so if an adenoma is present. It will be surprising what such management may, in certain cases, hold in store for a patient.

ANEMIA

The cardiac overaction of a patient who is very anemic resembles very closely the cardiac overaction of a toxic goiter patient. There are, however, some detailed conditions which serve to differentiate one from the other. Upon auscultation the first sound over the apex is not quite so loud and snapping as in the case of a thyroid heart. Moreover, a systolic murmur which is

usually present in these conditions is longer and softer in the case of anemia. There is no difference to the palpating hand. At any rate, by proper evaluation of all the available clinical and laboratory data there should be little, if any, trouble to differentiate cardiac overaction of anemia from that of thyroid origin.

FEVERS

In fevers the heart action is increased in intensity along with the rate acceleration, but again one should have little difficulty in making a diagnosis. If the impression is gained for one reason or another that a thyroid factor is present in a patient with temperature, it obviously follows that the suspicion must be disposed of in an orderly fashion.

In citing and discussing the exceptions above it may strike one that they are so numerous, complicated, and confusing that the sign of cardiac overaction in goiter toxicity loses much of its value. In reality the diagnosis of cardiac overaction is not difficult for one accustomed to making clinical examinations. It does, however, necessitate the skillful use of one's sense of feeling and hearing. In this connection I wish to commend an article recently published by Dr. James B. Herrick** in which he makes a plea in defence of the stethoscope and warns against its use becoming a lost art.

One can sum up the entire question by saying that first of all painstaking attention should be given to the study of the heart of every case examined.

**HERRICK, JAMES B.: "In Defense of the Stethoscope." *Annals of Internal Medicine*, p. 113, August, 1930.

Valuable clinical data will be derived from this practice. If it is continued year in and year out, slight variations from the normal will be detected almost instantaneously. If anything abnormal is detected, such study as is necessary can then be given it. If overaction is present, one can in a few moments make a mental survey of the conditions in which overaction occurs. They are after all few. By evaluating the characteristics of each, one should be able to determine with a reasonable degree of accuracy of what such overaction is an expression. One must always keep in mind that two, or even more conditions, may be present simultaneously. In the majority of instances the overaction will be found to be of

thyroid origin, at least in a goiter district.

The point I wish to emphasize is the presence of cardiac overaction at a time when the symptoms and signs generally understood to express thyroid dysfunction, are not yet obvious—in other words, in very early or mildly toxic cases*** and in atypical cases. The sign is valuable also after operation as being an indication of remaining toxicity. Because of its presence and constancy in practically all cases of goiter toxicity, it has been to me, for a number of years, the most helpful sign suggesting the presence of thyroid dysfunction.

***VANDEN BERG, HENRY J.: "How Long is a Toxic Goiter Toxic?" *Western Journal of Surgery*, 1930.

The Pituitary and the Suprarenal Cortex Glands as Related to Pigment Formation*

By ROBERT C. MOEHLIG, M.D., *Detroit, Michigan*

THE remarkable correlation of function between the various endocrine glands shows how well Nature has endowed our bodies with a complex mechanism. The unfolding of these correlations gives us an insight into many obscure problems.

For some time I have been working along embryological lines in order to solve some of the correlations. It is quite natural to look for a solution in embryology and much data have been supplied to support this hypothesis.

One of the most definite correlations is that of the pituitary gland and suprarenal cortex. In this particular correlation, we are treading upon firm ground, for we have clinical, pathological, experimental and embryological facts which prove beyond question that the state of the pituitary gland is shown by a similar state of the suprarenal cortex. Other articles¹ have shown that the embryohormonic relation of the pituitary to mesodermal tissues gives a clear-cut and logical explanation of the suprarenal cortex involvement, as the latter is a mesodermal tissue. The basis for these statements is found in hypo- and hyperplastic states of the pituitary which result in a

concomitant hypo- and hyperplastic state respectively, in the suprarenal cortex. Experimental work duplicating these clinical states of the pituitary, likewise produces the same concomitant condition in the suprarenal cortex. Cushing² agrees that the suprarenal cortex defect accompanying anencephalic states is unquestionably attributable to the absence of the pituitary. He goes on to say "It is interesting in showing this influence is present even in embryonic life, for I assume it is an experiment on the part of Nature comparable to what we may produce during life in the laboratory by extirpation of the hypophysis." We may safely say, then, that the state of the pituitary from a functional standpoint, carries with it a concomitant change in the suprarenal cortex. Aplasia or atrophy of the pituitary results in an aplasia or atrophy of the suprarenal cortex and the same holds true for the hyperplastic states. It is to be emphasized that the suprarenal medulla, an ectodermal tissue in contrast to the mesodermal cortical tissue, is not affected by the state of the pituitary. While this correlation provides an understanding for many problems such as cholesterol metabolism and related con-

*From the Department of Internal Medicine, Harper Hospital, Detroit.

ditions, it is the purpose of the present article to apply the fundamentals of this correlation to pigment formation.

Concerning the chemical mode of action on pigment and pigment cells of the pituitary and suprarenal cortex secretions, I can add nothing. But I hope the embryohormonic relations of the pituitary to mesodermal tissues as previously and herein given, will stimulate research by physiological chemists.

Assembled data has shown:

1. That posterior lobe pituitary extract is a melanophore stimulant.
2. That the suprarenal *cortex* occupies a high position in the physiological pigment production.
3. That the pituitary gland affects particularly mesodermal tissues.

We note from this that the pituitary gland and suprarenal cortex, which we know are definitely correlated, are concerned with the problem of pigment formation.

It has been known for some time that posterior pituitary extract is a melanophore stimulant. Smith³, Allen⁴, Spaeth⁵, Hogben and Winton⁶, Swingle⁷ and others have shown the stimulating effect of posterior pituitary extract on skin melanophores. Smith³ has done some excellent work on pigment changes in hypophysectomized tadpoles. These tadpoles become silvery white and Smith showed that the color changes are due to hormone action by affecting reciprocal epidermal transplants between "albino" and normal tadpoles. The chromatophores of the skin thus transplanted quickly assume the state of contraction or expansion characteristic of the corresponding cells of the host.

Only posterior pituitary extract produces a permanent darkening of the "albino." Of importance in Smith's work are his findings of a diminished suprarenal cortical material in the hypophysectomized "albino."

Hogben and Winton⁶ have shown that the action of the extract must be upon the pigment cell itself, as it acts upon the melanophores after paralysis of the nerve endings. Rowe⁸ working with "pitressin," a solution of the pressor principle isolated by Kamm and his associates, found that it stimulates frog melanophores.

Injection of posterior extract produces an expansion and darkening of the melanophores. Extract of one frog's hypophysis is sufficient to darken twenty to forty frogs. (Trendelenberg⁹).

The pigment cells of the frog iris expand and darken when immersed in posterior lobe extract.

An explanation of the melanophore effect of posterior extract may be found in embryological studies. The purpose would be to determine the embryological origin of the melanophores.

Bloch¹⁰ and his associates have studied the problem of pigment formation with particular reference to the embryological origin of the skin pigment cells. He defines melanoblasts as those cells which are capable of forming pigment, while those containing pigment which they themselves have not elaborated but have obtained elsewhere, (absorbed or phagocytized) are called chromatophores or melanophores. The mesodermal part of the skin, the corium, contains in man and in certain higher mammals, two entirely different kinds of pigmented cells. One

type are connective tissue cells which have phagocytized pigment which was originally formed in the epidermis. Another type which is found in the cutis, are the mesodermal melanoblasts, which he calls "Mongol" cells. They elaborate their own pigment, entirely independently of the epidermal pigmentation and embryologically long before this latter has appeared.

He says that the so-called blue nevi are large or circumscribed moles, which differ from ordinary brown moles in their blue color. As the cells of these blue nevi are mesodermal melanoblasts, the malignant growths which originate from these moles, are therefore true melanosarcomata.

Ribbert¹¹ many years ago was the greatest defender of the view that connective tissue gives off pigment cells and likewise believed that the nevus elements and melanotic pigment in general are derived from chromatophores and therefore are mesodermal in origin and that these cells stand in direct physiological relation to pigment formation. Borst¹² likewise supports this view. Naturally the relationship of physiological pigmentation is interesting in regard to melanotic tumors.

My purpose is to bring into physiological relationship the pituitary gland and the mesodermal pigment cells. Bloch¹³ gives as his opinion that the melanophores of the frog are mesodermal in origin. Ewing¹⁴ says: "The evidence accumulating in recent years from the comparative study of the physiology of the color function in the animal kingdom is a very formidable argument in favor of the specific mesoblastic nature of the chromatophores." With this evidence at hand, the em-

bryohormonic relation of the pituitary to mesodermal cells, provides a self evident explanation for its melanophore effect.

It affects specifically mesodermal cells and therefore the darkening effect of the mesodermal melanophores by the extract is explained. By the same token, the "albinous" effect of hypophysectomy is also explained.

The suprarenal cortex, correlated with the pituitary gland, which as we have seen affects pigment cells, occupies a high position in physiological pigment formation. Such studies force one to the conclusion that pigmentation is a metabolic phenomenon.

Jaeger¹⁵ studying melanosarcoma in grey horses had made some interesting observations on pigment formation. He found that melanosarcoma attacked practically only those horses whose hair had been either black or brown and then turned grey. He says that of great interest is the influence of the suprarenals on pigment formation. He is of the opinion that the suprarenal cortex, and particularly the cells of the zona fasciculata are responsible for the typical melanin formation. It has been shown by experiments that melanin production is a product of the suprarenal cortex. It has usually, but erroneously, been believed that the melanin is a product of the suprarenal medulla and chromaffin system.

It has been found that the epidermis of the grey horse is light in color, as well as the hair itself, so that there seems to be an intimate relationship between pigment effects of the body covering and the predisposition to melanosarcoma. In his studies on horses he finds that in melanotic sar-

coma there is a paralleling of the two processes, viz. a proliferation of connective tissue and fibroblast cells and an enlargement of the suprarenal cortex.

Melanosarcoma of the grey horse is an expression of a metabolic anomaly. Jaeger believes an abnormal pigment metabolism is present which releases the specific "melanogen" ferment producing an intracellular oxidation by means of the suprarenal cortex ferment. There is a conversion of the melanin by suprarenal cortex substance. Parallel factors are at work, pigment changes and the cell hyperplasia.

Ewing¹⁴ says: "It follows that there must be a close parallel between physiological formation of pigments and that seen in pathological conditions, such as melanosarcoma. Much evidence has been collected which points to the metabolic origin of pigment."

From the data at hand, it is evident that the suprarenal cortex is a factor in pigment production. The chemistry and its mode of action, are still unsolved. We have, therefore, two glands that are concerned with pigment formation; the pituitary which has an embryohormonic effect on mesodermal tissues, and the mesodermal suprarenal cortex, which mirrors the state of the pituitary.

The embryohormonic relationship between the pituitary gland and the suprarenal cortex leads us into the study of physiological pigment formation and that seen in tumor pigment formation.

Certain clinical facts furnish interesting proof of the pituitary and sup-

rarrenal cortex influence on pigment formation.

The darker races, such as the negro, should have a more active pituitary than the Caucasian, accepting this in the sense of the race as a whole. The negro, should also show, by the same reasoning, a more active mesodermal tissue involvement. His constitutional make-up should show a greater vulnerability of the mesodermal "anlage." Therefore hypo- and hyperplasia of these tissues with resulting clinical symptoms should be very common in the negro.

The mesodermal suprarenal cortex, mirroring the state of the pituitary, is found to be much larger in the negro. (Jaeger¹⁵). Is this why the negro seldom has Addison's disease?

Connective tissue, another mesodermal tissue, shows a greater overgrowth in the negro and the tendency to keloid formation is also well known.

We are well aware of the fact that neurofibromata originating in the mesodermal fibroblasts are a very frequent finding in acromegaly. (Von Recklinghausen's disease).

The mesodermal dentin and cementin accounts for the excellent formation of the teeth, for which the negro race is famed. The overgrowth of the mesodermal smooth muscle, as in the uterus, may account for the high incidence of fibroids in this race. The mesodermal sex glands are notoriously well developed in the negro. The early maturity of the darker races and the supposedly greater libido of these races could be understood from this. The predisposition of the negro race to luetic aortitis (mesodermal blood vessels) is also common knowledge.

Then too, in acromegaly and gigantism, we find telangiectasis (mesodermal blood vessels) (Grünfeld¹⁶, Bigler¹⁶, Lehman¹⁶) and also abnormal pigmentation of the skin. Uebelin¹⁶ notes the frequent formation of tumors in the skin of acromegalics.

Further argument of the negro race's mesodermal vulnerability is shown by the fact that this race has an affection strictly limited to them. I refer to the involvement of the red blood cells in sickle cell anemia. Negroes, on the other hand, seldom have pernicious anemia.*

It is interesting that with such a high incidence of syphilis, paresis and tabes are not as frequent in the negro as in the Caucasian race. This again demonstrates that the ectodermal system is not so vulnerable.

The mesodermal bone tissue frequently shows abnormalities. Gigantism, dwarfism, rickets and achondroplasia are often met with in negroes, the dwarfism being characteristic of the pigmy race in Africa. It is a well known fact that the Caucasian race, when acromegaly develops, takes on the coarse features and characteristics of the negro tissues.

It would be interesting to see if acromegaly ever develops in the blond and if so to note the change in hair and skin pigment. The hair papilla and outer sheath are of mesenchymal origin and influenced therefore by the pituitary gland. The marked hairiness of the acromegalic is understood on this basis, as well as the lack of hair in the hypopituitary individual.

*Ewing says he has never seen melanoma in a negro. (Personal communication).

In hypopituitarism in contrast to hyperpituitarism, the skin is poorly pigmented and the effects of the sun rays and other actinic influences are much more severe in these people.

It follows that hyperpituitary individuals should have many pigment anomalies of the skin and iris. This is true clinically. The negro of course has a darker sclera than the white race. The ophthalmologists could solve many eye disturbances if attention was paid to the embryological origin of the layers of the eye with reference to the selective action of the pituitary on mesodermal tissues and particularly to mesodermal pigment diseases. Such fundamental studies become of greatest importance to medical progress.

From what has gone before it becomes almost an inevitable corollary that the pituitary gland and suprarenal cortex are the responsible factors for the pigmentation of pregnancy. The pituitary forms at this time the well known "pituitary of pregnancy," and the suprarenal cortex becomes hyperplastic during pregnancy.

The embryohormonic relations of the pituitary to mesodermal tissues give a most rational explanation of pigment formation and a most reasonable explanation for many pigment changes.

SUMMARY

Both the pituitary gland and the suprarenal cortex are concerned with pigment formation. The embryohormonic relations of the pituitary to mesodermal tissues explains the melanophore action of posterior lobe extract. The mesodermal suprarenal cortex, reflecting or mirroring the state of the pituitary is also concerned with

pigment formation. The negro race with a comparatively more active pituitary gland is constitutionally predisposed to disease affecting mesoder-

mal tissues. The pituitary gland and suprarenal cortex are probably responsible for the pigmentation of pregnancy.

REFERENCES

- ¹MOEHLIG, ROBERT C.: A Study of the Ductless Glands, *Detroit Med. J.* 14:268-289, 1914; Ductless Gland Cell Control, Monograph, 1918, pp. 87; Selective Tissue Action of Posterior Pituitary Gland; *Med. Jour. & Rec.* 120: (Aug. 20) 55-59, 1924; Selective Action of the Suprarenal Cortex on Mesothelial Tissues, *Am. J. M. Sc.* 168:553, 1924; The Antagonistic Action between Insulin and Posterior Lobe Extract. *J.A.M.A.* 84:1398, 1925; MOEHLIG, R. C., AND AINSLEE, H. B.: Posterior Pituitary Extract and Cholesterol Metabolism, *Am. J. Phys.* 80:649, 1927; MOEHLIG, R. C., AND AINSLEE, H. B.: Pituitary Gland and Cholesterol Metabolism, *Ann. Clin. Med.* 5:772, 1927; MOEHLIG, R. C.: Embryohormonic Relations of the Thyroid Gland to Ectodermal Tissues. *Ann. Int. Med.* 1: 400, 1927; Embryohormonic Relations of the Pituitary Gland to Mesenchymal Tissues, *Ann. Int. Med.* 1:563, 1928. Embryohormonic Relations of the Suprarenal Cortex to Mesothelial Tissues, *Ann. Int. Med.* 1:828, 1928; Pituitary Gland and Suprarenal Cortex, *Arch. Int. Med.* 44: 339, 1929.
- ²CUSHING, H.: Personal Communication.
- ³SMITH, P. E.: *American Anatomical Memoirs*, No. 11, 1920.
- ⁴ALLEN, B. M.: *Anatomical Record* 11:486, 1916.
- ⁵SPAETH, R. A.: Concerning a New Method for the Biological Standardization of Pituitary Extract and other Drugs. *J. Pharm. & Exper. Therap.* 11:209, 1917.
- ⁶HOBEN, L. T. AND WINTON: The Pigmentary System. Reaction of Frog's Melanophores to Pituitary Extracts. *Proc. Royal Society, Biol. Sciences (Series B)* 93:318, 1922.
- ⁷SWINGLE, W. W.: Transplantation of the Pars Nervosa of the Pituitary, *Anat. Rec.* 23: 125, 1922.
- ⁸ROWE, L. W.: Studies of Oxytocin and Vasopressin; The Effect on Frog Melanophores. *Endocrinology*, 12: 663, 1928.
- ⁹TRENDELENBERG, P.: *Die Hormone*, Julius Springer, Berlin, 1929, p. 158.
- ¹⁰BLOCH, B.: Problem of Pigment Formation, *Am. J. M. Sc.* 177:609-618, May, 1929.
- ¹¹RIBBERT: Quoted by Jaeger. Ref. 15.
- ¹²BORST: Quoted by Jaeger. Ref. 15.
- ¹³BLOCH: Personal communication.
- ¹⁴EWING, J.: *Neoplastic Diseases*, W. B. Saunders Co. Phila, 1922, p. 872.
- ¹⁵JAEGER, A.: Melanosarcoma of the White Horse. *Arch. f. Path. Anat.* 198: 105, 1909.
- ¹⁶GRUNFELD, ETC.: Quoted by Bauer J., *Konstitutionelle Disposition zu inneren Krankheiten*. Julius Springer, Berlin, 1924, p. 302.

Thoracic Aneurysm

Statistical Study of Seventy-one Cases*

By SHELTON P. SANFORD, A.M., M.D., *Atlanta, Ga.*

THE object of this paper is to present a statistical study of cases of aneurysm of the thoracic aorta at the Grady Hospital, Emory University Division. A series of seventy-one was selected. Necropsy was performed in thirty-two of these. A number of cases have been discarded because the diagnosis seemed uncertain and necropsy was not done. All patients were colored.

The seventy-one cases have been studied with regard to the following twenty-two points:

1. Age
2. Sex
3. Admission Diagnosis
4. First Symptom
5. Chief Complaint
6. Duration
7. Initial Lesion
8. Wasserman Reaction
9. Roentgenograms
10. Aortic Second Sound
11. Cardiac Irregularities
12. Abnormal Pulsations
13. Inequality of the Pulse
14. Blood Pressure
15. Hoarseness
16. Dysphagia
17. Tracheal Tug
18. Hemoptysis
19. Inequality of the Pupils
20. Glandular Enlargement
21. Cause of Death
22. Necropsy

(1) *Age.* The youngest of the group was 22 and the oldest 80. Arranged according to age there is a rise at 40 which represents the age of greatest frequency of disability from aneurysm. There is a rapid fall to 50. After 50 there are only sporadic cases up to the age of 80. The average time interval from initial lesion to onset of symptoms is slightly over fifteen years. There is also a small peak at 26. I believe this peak probably represents cases of acute syphilitic myocarditis associated with small aneurysms of the sinuses of Valsalva. This group will be made the subject of a separate paper.

(2) *Sex.* In the series of 71 cases there were 54 men and 17 women. This proportion of women is larger than in textbook statistics. It includes perhaps, a few cases of non-syphilitic rupture of the aorta.

(3) *Admission Diagnosis.* An analysis of the diagnoses on admission in proved cases of aneurysm has been made in an effort to point out some of the pitfalls of diagnosis. In 30 of the series the correct diagnosis of aneurysm was made. The diagnosis of aortic regurgitation was made nine times. This was usually done on the murmurs alone. When murmurs simulating aortic regurgitation exist with-

*From the Emory University Division, Grady Hospital.

out a Corrigan pulse, low diastolic pressure and other peripheral signs of aortic regurgitation, one should strongly suspect aneurysm. Three cases were diagnosed pulmonary tuberculosis. An examination of the blood pressure would have helped exclude this error. Most cases of pulmonary tuberculosis show a systolic blood pressure of 110 with a diastolic of 70 or lower, while cases of aneurysm with pressure on the trachea show higher pressure until the last stages of the disease. One case was diagnosed chronic adhesive pericarditis, probably on account of murmurs.

TABLE OF ADMISSION DIAGNOSES

Aneurysm	30
Aortic Regurgitation	9
Mediastinal Tumor	3
Pulmonary Tuberculosis	3
Hypertension	2
Bronchitis	2
Cardiac Asthma	1
Mitral Stenosis	1
Aortic Stenosis	1
Pneumonia	1
Carcinoma of Lung	1
Laryngeal Obstruction	1
Syphilitic Heart Disease	1
Auricular Fibrillation	1
Syphilitic Aortitis	1
Tuberculous Laryngitis	1
Congestive Heart Failure	1
Tabetic Bladder	1
Dementia	1
Acute Alcoholism	1
C. N. S. Syphilis	1
Duodenal Ulcer	1
Peritonitis	1
Chronic Adhesive Peritonitis	1
Cirrhosis of Liver	1
Renal Calculus	1
Osteomyelitis	1
No Diagnosis	1

The correct diagnosis was the most frequent one. In some of the other cases two conditions coexisted and the

symptoms produced by the aneurysm were negligible or entirely overshadowed by an acute disease. By an examination of the table it is seen that in 31 of the incorrectly diagnosed cases the symptoms were cardiorespiratory and directly attributable to the aneurysm. In 4 cases the outstanding symptoms pointed to the central nervous system and in 3 of these the immediate cause was the aneurysm. In the fourth paresis coexisted. In the remaining, aneurysm was incidental to other diseases.

(4) *First Symptom.* The first symptom of the illness leading to the diagnosis of aneurysm was investigated in 68 cases. The distribution was as shown in the following table:

Pain in chest	25
Dyspnea	23
Cough	8
Dysphagia	3
Palpitation	1
Asthma	1
Enlarged gland	1
Vertigo	1
General malaise	1
Hoarseness	1
Convulsions	1
Syncope	1
Ascites	1

The table needs little comment. In a large majority, 61, of the cases the first symptom directed attention to the chest.

(5) *Chief Complaint.* The presenting symptom was examined in 70 cases.

Dyspnea	29
Pain	22
Dysphagia	3
Tumor	2
Cough	2
Angina	1
Asthma	1

Hoarseness
Unconscious
Acute retention urine
Dimness of vision
Dementia
Abdominal cramps
Osteomyelitis
Epistaxis
Ascites

1 of the series. There was sufficient
2 abnormality present at least to sug-
1 gest aneurysm in 47. No examination
1 was made in 10. In 14 cases there was
1 no reason to suspect aneurysm by
1 roentgenograms alone. It must be re-
1 membered that small aneurysms situ-
1 ated in the pericardium will not be
shown roentgenographically. It is this
group which gives the greatest trouble
in diagnosis and is usually found only
at necropsy.

In 61 of the 70 cases the chief complaint was one which should have directed attention to the cardiorespiratory system. In 5 the presenting symptom suggested a C. N. S. lesion. In 4 of these the aneurysm was responsible for the symptomatology. In 4 the presenting symptom was such that the diagnosis was not even remotely suggested.

(6) *Duration.* The duration of symptoms before fatal termination was investigated in 40 cases. It varied from one day to seven years, but in the majority of cases death followed within three months after the onset of symptoms.

(7) *Initial Lesion.* In 35 cases of the series a definite history of an initial lesion, with adenopathy was obtained, and the shortest period between the primary sore and the earliest symptom suggesting aneurysm was two years, the longest was 50. The average in the 35 cases was 15 years.

(8) *Wasserman Reaction.* The Wasserman reaction on the blood was positive in 50 of the 71 cases, negative in 11 and not mentioned in 10. This represents a positive Wasserman reaction in 82 per cent of the cases where the test was reported.

(9) *Roentgenograms.* A roentgenographic examination was made in 61

(10) *Aortic Second Sound.* There has been much written about the accentuation of the aortic sound in syphilitic aortitis and aneurysm. It is recorded as present in 37 of this series, replaced by murmur in 8, absent in 8, and not mentioned in 18. In our experience, in the absence of well marked hypertension, an accentuated aortic second sound is a most reliable sign of aneurysm. Fortunately, when hypertension and aneurysm coexist, other signs help to make the diagnosis clear. The diastolic shock often associated with thoracic aneurysm is merely a palpable aortic second sound.

(11) *Cardiac Irregularities.* Irregularity of the heart was noted in 20 of 61 cases. In 10 of the 71 cases the point was not noted. In 19 the irregularity was classed as frequent or rare extrasystole and in one, auricular fibrillation. This point is worthy of special attention as the number is considerably larger than one would expect in a group of 71 unselected hospital patients.

(12) *Abnormal Pulsations.* These were noted in 49 of the 71 cases. No abnormal pulsations were noted in 12, and in 10 the fact was not recorded.

This appears a rather low proportion, but when it is recalled that the series includes a case of transection of the cord, producing paralysis of the bladder, and yet no visible pulsation, it is not so surprising.

(13) *Inequality of the Pulse.* This has been given much space in textbooks as a sign of aneurysm. In this series it was noted only 9 times and then only in advanced cases. When present other signs of aneurysm usually overshadow it. Unequal pulses are more frequent from other causes, as an anomalous radial artery. As an aid to diagnosis I believe its importance overestimated. However, a weaker pulse which is also a delayed pulse is occasionally a very striking and important sign of aneurysm.

(14) *Blood Pressure in Aneurysm.* One is not surprised to find a wide range of blood pressure in aneurysm. There is not a preponderance of cases with hypertension. I have observed an eroding aneurysm on a syphilitic basis with a systolic blood pressure of 180 and diastolic of 120. I think this must be considered a case of hypertension which subsequently developed an aneurysm.

The curves on blood pressure would be more instructive if they could all have been studied in the same stage of advancement. Many of the series are advanced cases, and many are terminal cases and have no blood pressure readings. (See accompanying graphic representations).

If the blood pressure readings are arranged on an average curve it is found that the apex of the systolic curve is reached at 140 and of the

diastolic at 90. This I believe the most common blood pressure reading for aneurysm of the thoracic aorta. Such a blood pressure reading in a syphilitic subject, complaining of pain in the chest and dyspnea, should make one strongly suspect aneurysm.

TABLE V
TABLE OF BLOOD PRESSURE

SYSTOLIC		DIASTOLIC	
Above 210	3	140-150	0
170-180	4	130-140	0
160-170	3	120-130	3
150-160	4	110-120	3
140-150	5	100-110	9
130-140	18	90-100	10
120-130	7	80-90	11
110-120	7	70-80	9
100-110	8	60-70	7
90-100	0	50-60	4
80-90	2	40-50	1
70-80	1	30-40	1
60-70	0	20-30	0
50-60	1	10-20	0

(15) *Hoarseness.* This occurred in 30, not present in 26 and not mentioned in 15 of the series. It was the first symptom in one case. When present, there are usually more outstanding signs and symptoms. One would hardly be justified in suspecting aneurysm on so common a symptom without supporting evidence.

(16) *Dysphagia.* Was present in 14 cases, absent in 47, and not mentioned in 10, and was the presenting symptoms in two cases. While 14 is a relatively small number of the 71, still when present, dysphagia is a very striking symptom and it deserves all the attention given it in literature.

(17) *Tracheal Tug.* First observed by Oliver, has been noted in 12 of this series, absent in 47 and not mentioned in 12. It has not been of much help

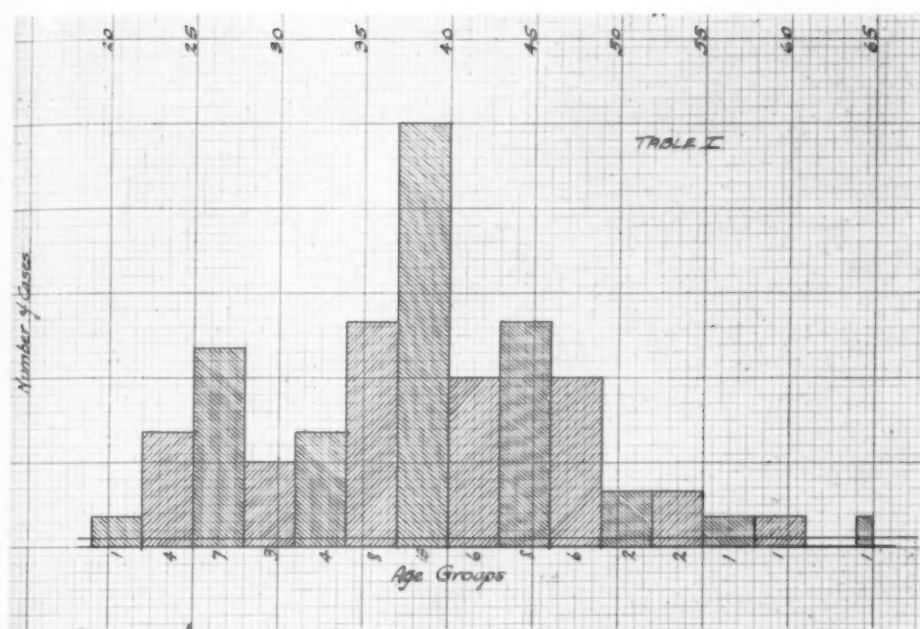


CHART I. Distribution of cases by age groups.

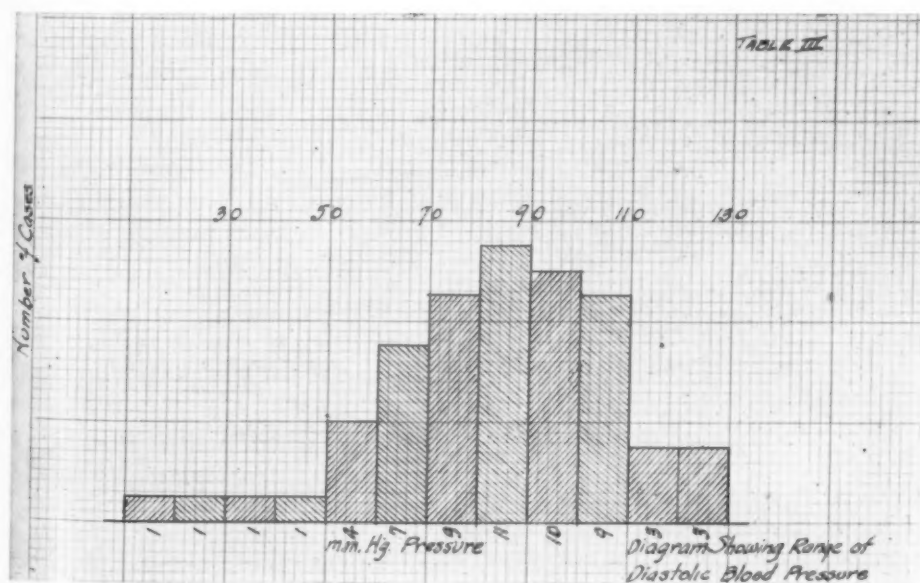


CHART 2. Range of diastolic blood pressure.

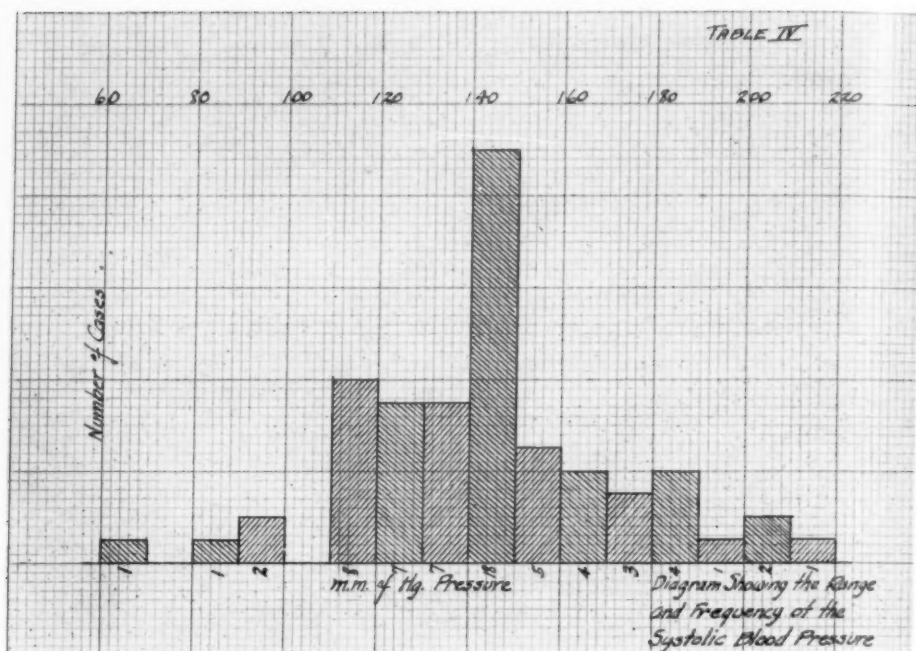


CHART 3. Range of systolic blood pressure.

in diagnosis. It is present only in those cases pressing on the trachea and primary bronchi. Other signs usually overshadow it. It is not nearly so important as the accentuated aortic second sound and the character of the blood pressure.

(18) *Hemoptysis*. Spitting of blood occurred only 12 times in the course of the disease in our 71 aneurysms. It has never been the presenting symptom nor the immediate cause of death.

(19) *Inequality of the Pupils*. This was formerly supposed due to aneurysm, but now generally attributed to cerebrospinal syphilis, old iritis, etc. It has not been of much assistance in diagnosis in this series. There must be a few cases of aneurysm which present a true Horner's syndrome, but they are not of frequent occurrence.

In this series the pupils were normal in 46, abnormal in 13, and not mentioned in 12.

(20) *Glandular Enlargement*. A general glandular enlargement was noted in 42 of our series, not present in 11 and not mentioned in 18. It will be seen this compares favorably with the positive Wasserman reactions. It is well known that in some cases of late syphilis, glandular enlargement is no longer present, though this may have been present in the earlier stages. However, one is impressed with the large number of cases of persistent glandular enlargement in this series of aneurysm.

(21) *Cause of Death*. This was known in 41 of the series. They are grouped as follows:

Rupture	17	is a corollary of Cabot's observation
Suffocation	9	that the heart is rarely enlarged in un-
Chronic Passive Congestion	7	complicated aneurysm. One is im-
Post Operative	3	pressed with the larger number which
Pneumonia	2	died of pressure on the trachea and
Multiple Pulmonary Infarctions	1	consequent suffocation. These cases
Cirrhosis of Liver	1	are prone to die earlier than those
Mesenteric Thrombosis	1	which grow expansively and rupture.

From this table of causes of death, it is seen that about 42 per cent died of rupture. This corresponds with the experience of others who have collected statistics on aneurysm. One other fact is worthy of note. Only 7 died of congestive heart failure. This

(22) *Necropsies.* Necropsy was performed on 32 of the 71 cases. In the other cases the diagnosis has been quite obvious through physical signs and roentgenographic examination.

Chronic Pulmonary Infections in Childhood*†

By ALLEN K. KRAUSE, *Tucson, Arizona*

FOR years our withers have been wrung by an unremitting chorus of concern over the sad, yes, the desperate case of the child with tuberculosis. One with a fair memory need not ask for particulars. Most of us here whom age is beginning to beckon set out to practice medicine with the fixed idea that a tuberculous baby must die, a preconception that, to my knowledge, bore fruit in a pediatrician of repute preparing an aspiring and unsuspecting mother for the inevitable by solemnly, yet as gently as possible, informing her that her flourishing young heir of six months, off color for the day, could not survive into childhood—all on the strength of a positive Pirquet test. This eminent physician will soon no doubt be ministering to the children of the baby he years ago condemned to certain and early death, a baby who compassed a healthy childhood and vigorous adolescence, and now knocks at manhood's portals, still Pirquet positive, we suspect, but enviably healthy.

With the dismal dogma of inevitable fatality of infantile tuberculosis went the no less upsetting one of ex-

ceptional susceptibility of the child to the disease and of slim resistance to it when acquired. Our knowledge of tuberculosis in early life has expanded vastly, and sent down more and more sound and solid foundations since monographs and textbooks began to labor the thought and enforce the natural inferences to be derived from it. Today the concept seems to be as firmly entrenched as ever; in support of which supposition we need only point to the fact that for the last few years the plight of the child in this world of tubercle bacilli—a rapidly contracting one, by the way—has been bruited as the chief *casus belli*, the most telling call for action in organized anti-tuberculosis effort.

Few labors in this terrain of fleshly infirmity can be more worthy than the struggle against tuberculosis that has aroused the unselfish aspirations of entire nations of modern times to stamp it out. But, after we have got used to working up our own lather and that of the tender-hearted by fervid appeals to sympathies that stand aghast at accounts, in the name of science, of defenseless childhood, it is disconcerting to work over plain and elementary facts that refuse to fit in with the accepted doctrine. Briefly, there is evidence, and plenty of it, that infancy and childhood are inherently not so

*From the Desert Sanatorium and Institute of Research, Tucson, Arizona.

†Presented at a meeting of the Southwestern Pediatric Society, Los Angeles, California, December 15, 1930.

powerless against tuberculosis. Moreover, a growing understanding of tuberculosis in early life and, indeed, of tuberculosis at all ages, casts increasing doubt on any idea of unusual or excessive susceptibility to tuberculosis during the formative years. Finally, the chief support of such an idea has come from opinions formed long ago, when our knowledge and comprehension of tuberculosis were relatively quite imperfect.

For instance, the time was not so long ago—it was within the lifetime of many of us, that authorities were disputing the identity of tuberculosis of certain regions with a disease called scrofula; that a few men, well in advance of their day, were timidly suggesting that pulmonary tuberculosis was a not infrequent form of the disease in early life, as others, representing the weight of opinion, made of it an exclusively adult type; that to medicine at large real tuberculosis in infancy and childhood meant meningitis and generalized miliary disease; and that any idea of concealed, or non-active, or obsolescent tuberculosis at these ages simply did not exist.

The results of observations in such a simplified realm of tuberculosis, the inferences drawn, the concepts formed, the doctrines erected, were natural, logical and plain. When a physician's view of the disease was restricted to meningitis and the miliary type, he had, of necessity, to conclude that that disease must terminate fatally, just as would his modern brother today in the same circumstances. But tuberculin testing and bacteriological investigations and X-ray observations give the modern confrère tools that no longer

allow him to so circumscribe his appreciation of tuberculosis. Little by little, yet not so extensively nor so alertly as he ought, he has widened the boundaries of what has come to stand for tuberculosis. The meaning of scrofula has become settled. The lungs of infants and children provide focal soil for tubercle bacilli as frequently as do those of adults, while their lymphatic adnexae emerge as the most common of reservoirs for infection. The skin, the eyes, the ears, the enteric lymphatics add enormously to regions where tuberculous effects may commonly be found. Tuberculosis in the infant and child becomes as far-flung as in the adult, in whom pulmonary involvement is the type of tuberculosis, active, and even more so: far-flung, yet not in the sense of generalized miliary disease, with progressive foci everywhere. As we become alive to possibilities, we find child after child with tubercle at several locations—pulmonic hilum, lung, conjunctiva, skin, and perhaps bone or joint thrown in for good measure—yet in constitutional health that is merely indifferent.

We have advanced to a point where we can appreciate how tuberculosis in infants and children is repeating the same experience, as regards our comprehension of it, that it has undergone for every part of the body. Broadly, we can lay it down that the prognosis of tuberculosis anywhere—of any and every part of the body—improves in direct proportion to our ability to recognize it. It was so for the lungs, then for the larynx, and now for the intestines, and who can say that it will not be so for the men-

inges? And the case is no different for infants and children.

If, let us say, the diagnosable cases of tuberculosis of the lungs were still restricted to those that would yield to Laennec's methods of detection, it is doubtful whether our vaunted superior modes of treatment would save many more patients than were rescued by Laennec and his followers. For, to Laennec the "case" of pulmonary tuberculosis began at a stage now regarded as far advanced and, in general, hopeless. But the century following Laennec saw the boundaries of this clinical condition pushed to an extent that they not only embraced types of tuberculous infections that would heal themselves, but even promised to include, and actually did include, types that would likely never set up a condition that required treatment. Similarly, the outlook for tuberculous enteritis has lately improved enormously, as by refined roentgenology we manifold our cases, and so take credit for curing a large proportion, which, not much longer than ten years ago, were healing themselves as they passed unnoticed.

In like manner we have widened the field of tuberculosis in childhood. Proceeding naturally from the more apparent to the more concealed, we have added condition after condition of tuberculous infection, to indicate the existence in early years of ever more benign states—types—of the infection. We have now gone far enough to be able to say that, by and large, tuberculosis, as such, is essentially a non-progressive infection in not only the adult, but in the child also, and, un-

less all signs fail, in the infant likewise—if not no less.

By this we mean to set down our belief that, if the truth as to incidence of tuberculous infection were known, we should find that, though actual proportions might differ, all periods of human life would exhibit a great preponderance of benign, that is, non-progressive, non-clinical, non-active tuberculous infections over progressive, clinical, active ones. Indeed, after one has tried to account for the several variables of environment, as these are known and presumed to influence tuberculous infection and its results, and as they may operate differently at the different periods of life, one will likely find little to support a thesis to postulate a greater innate defenselessness toward tuberculosis during human life's tender years.

As for the period of childhood, all signs point to a condition of extraordinarily high resistance. Childhood is really mankind's "golden age" as regards tuberculosis. Enlarging spheres of activity and experience multiply contacts for the infant emerging into childhood and the child on its way to adolescence; whence, ever-increasing opportunities for infection, numerically if not quantitatively. Yet the results are not what would be expected, and they could hardly be predicted.

First, the mortality from tuberculosis falls sharply from that maintained in infancy; and soon reaches a nadir that is maintained until late childhood, when the rise to the mortality peak of manhood begins. Never before and never again afterward do we find such low tuberculosis death rates as obtain in childhood; and this too is the period

when opportunities for infection are most common and infections are being received most frequently. If it were a period of peculiar freedom from disease and respiratory disorders and ill health in general we might grasp at the circumstance to explain the paradox of declining mortality with mounting infection. But childhood is not such a period. It is the very reverse, and is withal that time of life when any consciousness as to personal cleanliness and bodily care is at its lowest and when these needs are least looked after.

Again, the morbid effects of the tubercle bacillus in the child are ordinarily of a kind to suggest unusual tolerance for the bacillus. Tuberculides and other eruptions of tuberculous origin bespeak a dissemination of bacilli throughout the body: they are a frequent occurrence in children with health but slightly if at all impaired. The same thing may be said for phlyctenular conjunctivitis and keratitis, especially when combined with tracheo-bronchial lymphatic and perhaps cervical lymphatic involvement, associated too with the perennial Ghon focus: the bacillus has made the rounds of the body, has focalized appreciably at several remote points and presumably at numerous other points, yet the child is so slightly affected that in the circumstances only too many physicians centre all attention on tonsils and adenoids. One's amazement grows with one's experience with what in the way of tuberculosis the child will often tolerate in the lungs, and maintain fair health throughout. The bone and joint foci that remain localized and are recovered from far exceed those that

break through and spread to a fatal termination. The abdominal lymphadenitides and the peritonitides that heal again outnumber those that erupt to generalized miliary disease and meningitis. Indeed, grade for grade, matching focus with focus and locus with locus, it is questionable whether the adult will compete with the child against the onslaughts of tuberculosis. My own opinion is that the child "has the edge." When we get down to examining more ailing children for pulmonary tuberculosis, and diagnosing more of them with the slight changes that are sending adults to the sanatoria, we shall know more about all this. At this juncture I would merely make a passing plea for a general recrudescence of tuberculin testing in pediatrics practice. I imagine, too, that a cardinal rule of diagnosis in internal medicine can be no less fruitfully applicable for children: to wit, that the more obscure an ailment, with earmarks of an infection, remains, as one after another diagnostic test falls short, the closer one is approaching to a diagnosis of tuberculosis. And it is here that tuberculin's evidence grows most compelling; for a positive test gains in meaning as other possibilities dwindle.

I am not taking this attitude toward tuberculosis in children with the intention of belittling its gravity. I do so mainly to drive home the point that in early life tuberculosis may, and perhaps the more frequently does exist, in its benigner forms; that the physician should be alive to this common occurrence; that he should divest himself of any idea that tuberculosis is an impossible diagnosis unless he is con-

fronted by serious physical manifestations; and that, if the truth were known, the more common clinical presentation of tuberculosis in early life appears to the physician as the hardly sick child, or the lackadaisical child, or the transitorily upset child, or merely the overirritable child. Tuberculosis in children can have its unmistakable syndrome just as it can have in adults, but, again as in adults, it can throw out its warnings in the most unexpected and most equivocal of guises, and a resistant soil in childhood can yield a no less abortive and stunted harvest of physical changes.

Again, as in adults, tuberculosis in children at any time may or may not be arousing physiological (functional) disturbance. If, when, and as long as it is deranging function, it must be regarded as clinically active, that is, worthy of medical attention and treatment, and, conversely, it passes outside the concern of medical practice if, when and as long as it does not and promises not to affect the bodily economy adversely.

Personally, I can comprehend no middle ground between tuberculosis active and tuberculosis inactive, as a matter of practical medical concern and as based on a concept of a demonstrable influence of existing tubercle on local or bodily (constitutional) function. At any time foci of tubercle are exerting a telling, an appreciable, influence on function, or they are not so operating. If they are, they are clinically active; if they are not, they are clinically inactive. The term "latent" has latterly come into vogue, but just what it is to express or imply has never been made clear. It obviously

does not essay to take over the well-understood connotations of inactive tuberculosis; it evidently shrinks from embracing attributes that we are wont to associate with activity. It seems in an indefinite way to define a state of tuberculosis that lies or wanders between activity and inactivity. But, is there any such *status quo*, changing perhaps, of tuberculous effect? And, if there is, would its formulation serve a useful practical purpose?

I have had it explained to me that "latent" tuberculosis defines and marks out that condition of tuberculosis in children that is likely to be missed by the average practising physician. But this can hardly be possible, for in actual existence it could have no fixed position in structure, in function, in methodology, or in the profession. I have myself got the impression that there was first created a particular symptomatology, with perhaps fever the crucial element, that was to stand for active tuberculosis, and that then any evidence of the stirrings of tuberculosis that fell short of this symptomatology, especially as the latter lacked fever, were to be denominated as "latent" tuberculosis. For instance, an underweight child, with certain tell-tale markings within the chest yet without fever and, let us say, also cough, was to be regarded as laboring with "latent" tuberculosis.

This would delight the users of the old term "pretuberculosis," especially if such a child came down later with tuberculosis full-blown and with classical signals unfurled. But, could anything be more misleading or more disserviceable in lulling the rank and

file of physicians into a false sense of their responsibility in the premises?

Let us imagine that undernutrition and only undernutrition in a child brings the latter to a physician's attention, and, moreover, that exhaustive examination discloses nothing to account for the inability to attain or maintain normal weight except a focus of tubercle. The next step is to prove that the focus is responsible for the bodily disturbance. If, now, this can be established, how can we regard the focus in any way other than that it is active? If tubercle so affects the body as to stunt it, or disturb nutrition, or set nerves over-irritable and a-jangle, or lower muscular or vascular tone, is not such an influence just as surely an evidence of deleterious effect as is the much more superficial one of disturbance of temperature? Should we not regard the disturbances mentioned as the deeper-seated by far, and therefore as surely the manifestations of "activity" as is a derangement of temperature, which is really rather incidental?

There is indeed no royal road to the diagnosis of tuberculosis, and in medical practice an expanding knowledge has made "tuberculosis" synonymous with "active tuberculosis." And the first step in the approach to this diagnosis is a grasp of the general principle that nowadays three particulars are always necessary to the conclusion. These are, first, that there is something awry, as signalized in a region, an organ, a body out of rhythm, let us say; second, that within the same organism lies specific tubercle disclosed; and, third, and most important, that the arrhythmia, the disharmony, the derange-

ment, can be brought into correlation with the tuberculous formation. Given these, and almost all aberrations of the flesh will take almost equal rank as harbingers of tuberculosis—of that tuberculosis that merits, that demands medical attention—of, if you please, active tuberculosis. Unwonted pallor will rank with cough; premature systoles, depressed blood-pressure, over-irritable heart with elevation of temperature; nervous over-irritability with undernutrition; and, usually, if not always, there will show through the cardinal symptom of tuberculosis—asthenia—loss of tone—whether of skeletal musculature, of vascular tree, of psyche, of special senses, or of digestive tract. With the presence of tubercle proved, any aberration that can be tied to it spells tubercle in only one form—"active tuberculosis." In the presence of tubercle a completely sound body, functionally speaking, guarantees inactive tuberculosis for as long as no derangement of the bodily economy rears its head. There is no middle ground—no "twilight zone" of pre-tuberculosis, of latency, of preparation or maturation or concoction, in a clinical sense, much as anatomical, structural shifts may be astir—changes under way within tuberculous foci, to at last reach a quantity or quality that stamps telling noxious effects upon the animal organism. The only reservation that could hedge this dogmatic generalization would have to account for the more or less permanent functional derangements set up by the residua, the healed remnants, of healed or competently invested tubercle of the past.

For the rank and file of physicians tuberculosis has far too much usurped

the field of attention to chronic pulmonary infections. They are still accustomed to give all too scant thought to the possibilities of other than tuberculous *focal* infections within the lungs of infants and children. Yet, in early life such focal changes of non-tuberculous origin and nature are anything but rare; they are damaging; even in their minor phases they can be a tremendous drag on the child's normal development; they frequently set the stage for a later life of inefficiency and invalidism. They create a situation that should be grasped better by the generality of the profession.

Bronchiectasis, when fully expressed, is so definite a condition, it has so characteristic a symptomatology, it has originated out of so stereotyped a set of conditions, it is withal pregnant with so serious an outlook for the child, that its almost complete recognition would seem to be assured and expected: that is, when, as just said, it is fully expressed. However, in medical practice one gets the impression that the natural history of bronchiectasis is quite otherwise. The percentage of correct diagnoses attending the adult bronchiectatic patient's first resort to medical advice must be amazingly low; and the disease ranks high as one commonly detected first by the consultant and specialist. With experience one's astonishment grows at the numerous patients rounding out their years at tuberculosis resorts and even in sanatoria, and being treated for pulmonary tuberculosis, all the while they display such prime features of non-tuberculosis as negative (for acid-fasts) sputum, involvement restricted to lower

lung, and disproportionately minor constitutional versus obtrusive local symptoms. Surely a few weeks should suffice to rule out tuberculosis in most of these cases; and again and again this time will be shortened by tuberculin skin tests that result negatively—if only the tests are done.

Sometimes these cases will turn out to be abscess; sometimes that non-descript condition that masquerades in text-books as "chronic interstitial pneumonia," if indeed there be any such pathological reality; but most often, I suspect, they express clinically the local and constitutional effects of damaged air-passages, expanded permanently and dilated at certain points, and scarred and exuding secretions that cannot find prompt or adequate evacuation. A muco-purulent sputum, of whatever amount, that fails to yield acid-fast bacilli on repeated daily examinations and that emanates from a patient without evidences of diffuse bronchial involvement but with signs of focal changes below mid-lung, should without undue delay send the physician to at least imaginings anent the presence of bronchiectasis. In most instances these imaginings need not be vague, nor will they be vain; they will be translated into reality.

I would disclaim all pretensions to an unusual or extensive experience with bronchiectasis. Yet it is just because my contact with it has not been exceptional that I am the more impressed by the stretch of time that is wont to elapse between the patient's onset of illness and his at last correct diagnosis of bronchiectasis. So often has this happened that I have long taught that for the adult the average interval

is to be measured in years. Proportionately, for children the case is no better. If anything, it is worse; which makes it all the more regrettable; for if ever there was a disease whose potentialities required its early diagnosis, that disease is bronchiectasis. It may not kill as surely as tuberculosis, nor as quick. It may not bring the patient low as soon and as often; indeed, an antithetical disproportion between local and constitutional symptoms is a feature that we have stressed as among the distinguishing marks of bronchiectasis and tuberculosis. But, grade for grade, and short of the bed-ridden stages, bronchiectasis can be (and is) far more disabling than tuberculosis, and only too often far more impeding and offensive as well, while as to permanent healing or relief from symptoms, there is no comparison—the curability and amelioration of tuberculosis at advanced stages are vastly ahead of those of bronchiectasis in its earlier phases.

Short of confirmed bronchiectasis, yet on the way to it, there must be an almost illimitable gradation of minor pulmonary changes of greater or less permanence. Established bronchiectasis is wont to challenge our therapeutic resources, and tax these to the utmost; and the average result of treatment of even its milder phases is but indifferent success. For this reason alone it is important to detect the disease early, and make every effort to stay its progress, but even then a wisdom born of experience makes us chary of promising too much. Here indeed is a situation that points to the great importance of recognizing in the lungs of children all focal changes of

infectious nature—spots of permanently damaged tissue, with potentialities for progression and for indefinite and prolonged residence of microorganisms—patches that may go on to bronchiectasis, not to mention abscess, or may, now and again, flare into acute bronchopneumonia. That the lungs of children are very frequently the abiding places of unnoticed and unsuspected non-tuberculous foci of infection we are convinced. That the fact should be more generally appreciated and acted upon in the circumstances we are no less certain. It would seem that much ill health in childhood that now passes for disturbances in the upper respiratory tract,—the nose, the throat, the ears, the tonsils, the sinuses—is actually and largely the expression of chronic intrapulmonary infection; and that, moreover, not a little of the bronchopneumonia of childhood occurs really as a rather incidental acute event, punctuating the much more prolonged course of a preëxistent chronic infectious process, and not as the primary incident that ushers in the chronic changes that we detect later.

We have come to believe that the guise taken by these chronic focal infections in children can be no less misleading and impenetrable than those assumed by tuberculosis. But, masking them most frequently perhaps is all that goes into what we call "oversusceptibility to catching cold," as common a complaint as brings the child to the physician.

Now, oversusceptibility to colds can be of every degree and duration. It can be the habit of years or the unexpected manifestation of a first winter—a series of nothing more disturbing

than recurrent snuffles and running nose, or a succession of repeated febrile attacks with bronchitic symptoms uppermost. It may yield readily to judicious attention to faults in the nasopharynx or tonsils, or to correction of improper habits and parental care. On the other hand, it may resist the most expert measures and regimens designed to curb it. After everything corrective and curative is done, there remains a discouraging number of children whose health is variably and materially impaired because of oversusceptibility to colds and its consequences. At least, this is the outstanding complaint as voiced by the parent who presents the child to the doctor.

Whether the child is just emerging from infancy, or is six, eight or a dozen years old, there is an almost stereotyped sameness to its story—its clinical history. Its trouble all started with a hard common cold, an attack of so-called "grippe" or "influenza," or one of the acute infections of childhood—whooping-cough ranks peculiarly high here, with measles also prominent. This happened several years ago, since when the child has never been the same as before. It has shown an increasing tendency to contract fresh colds. These begin with the first change of season to cooler weather, and have latterly been recurring to such an extent as to house the child for much of the winter and interfere seriously with schooling. Seizures of bronchitis, with fever, are becoming more severe and more prolonged, and between acute periods a chronic condition of cough has settled in. These repeated illnesses have begun to tell

on the child's general health, as shown by noticeable pallor and a falling off in tone, vigor and nutrition. Because of occasional symptoms pointing to ears or throat, these, with perhaps the sinuses have been looked into, and adenoids have been removed and a paracentesis of the ear performed once or twice for an intercurrent otitis media. But what is giving the parents most concern are at last undeniable evidences that normal physical development is suffering, and the idea that a now confirmed pallor, undernutrition and listlessness mark a declining resistance to the normal shocks and stresses of childhood that will eventuate in fresh colds. Efforts to protect the child against exposure almost invariably result in over-coddling, and thus the vicious circle is fortified.

Up to this point most children of this type will have not gone beyond the care of the general practitioner, the family physician, except for special work that may have been done by the otolaryngologist. They form a rather unsatisfactory part of the former's practice, as year succeeds year with slight if any improvement, and adolescence is hopefully awaited as a time for the child to outgrow its "delicate constitution," and with this its genius for catching colds. It is only when, as frequently happens, an overly hard "cold" strikes in, with now plain evidence that the lungs themselves are affected, that a real turn in events sets in.

The child falls ill with symptoms and signs that are unmistakeably those of bronchopneumonia, which send the physician to more assiduous attention to the chest. The involved spot, ex-

tending out and downward perhaps from the root, is determined; and, as the child recovers from the acute illness, this spot is found not to clear completely. Râles fade out only gradually, and not entirely until long after clinical recovery from the pneumonic attack; while, still more significant, X-ray changes in the involved territory persist long after the last pneumonic râle has disappeared. The child, meanwhile, has resumed its old habit of "delicate constitution" with chronic cough. To the attending physician its attack of pneumonia has made one important difference; in his opinion, this has left a remnant of unresolved tissue in the child's lung, a patch that bids fair to undergo fibrotic transformation. The course of events has been plain: the child's susceptibility to colds had at last laid him open to pneumonia, a first manifestation of pulmonary involvement, which, in its turn, has put its rather lasting mark upon the lung. Whatever of moment may happen to the child later will have had its origin in the permanent damage done by the pneumonia. This will date the real beginning of any progressive pulmonary process that the years to come may bring forth: that is, all this is as the physician sees it.

We have come to doubt so orthodox an explanation. When good fortune has presented the necessary positive evidence in a few cases of the type under discussion, this has been of a kind to show unerringly that, prior to the pneumonia and probably for years, there had been in existence an undetected patch of focal change, non-tuberculous in nature, in the child's lung. Roentgenography, done months

before the acute pneumonic phase, had made sure of this datum. Then, most important to an understanding of cases of this type, when the acute bronchopneumonia did supervene, it involved the lung in the identical territory that had long been under observation as manifestly diseased.

That is to say, during the more ordinary period of the child's general complaint of oversusceptibility to colds and for some time preceding its clinical bronchopneumonia, there had been under medical observation a region of abnormally increased density and exaggerated markings that extended from the pulmonic hilum outward and downward into the lung—a type of change that had been regarded as definitely pathological and had aroused suspicions of incipient bronchiectasis yet could not be substantiated as such, that is, as a process that had progressed that far. When now the bronchopneumonia appeared, this was localized in and to the region in question. Roentgenographically the observer beheld the picture of a preexisting focus of morbid change that had, as it were, slopped over into the immediate neighborhood; as, under the spur of acute exacerbation, it poured forth those elements that converted, for the time being, the immediate region into a pneumonic patch. An abnormal, shadowed density, already and ostensibly long in being, was extending its boundaries out into the surrounding pulmonic field, as it too was undergoing certain changes in quality. It was plain that the pneumonia was originating in an already present focus of diseased tissue.

When now, as happened in the usual time, the pneumonia cleared, there took place simply a retreat, a drawing in of the pathological shadow to approximately its old contour; until, after some weeks, it looked hardly different in size and "texture" from the density observed months previously, before the attack of pneumonia. The point made above was that ordinarily in practice such a patch would be regarded as having originated from an unresolved pneumonia; whereas, the truth is that the pneumonia but represented an acute incident occurring in the course of an essentially chronic focal process, an acute exacerbation of a more permanent non-tuberculous focal infection that at all points differed little from analogous episodes that so normally punctuate the course of chronic tuberculosis.

A growing experience has led us to believe that cases of this type are anything but rare; that, indeed, there is a condition of focal non-tuberculous infection in childhood that in frequency and gravity will rank with the better appreciated tuberculous infection and which, in essential features, bears many striking resemblances to the latter; moreover, that perhaps the most common approach to medical attention for these non-tuberculous focal infections will be through the complaint of unusual susceptibility to colds. It is indeed this prime feature that forms the main burden of my present thesis.

I have recently brought to my attention a case, the son of a physician, with a history of three recurrent attacks of bronchopneumonia, and also the story of oversusceptibility to colds that antedated the first pneumonia.

Fortunately, this boy's chest has been X-rayed at intervals since before his first acute upset. In all particulars his case repeats what was sketched in outline above: from the time of the first X-ray films there has been in existence an abnormal basal density, and every exacerbation of pneumonia has had its origin and its being in this territory. And now, to fill in these more or less ideal and composite descriptions with more concrete particulars, another actual case may be summarized briefly.

It concerned a youngster, five and a half years old, born into and bred in a home of wealth, comfort and intelligence, and exceptionally healthy and flourishing from birth until ten months old, when severe whooping-cough, to which the beginning of all present trouble is attributed. Since the whooping-cough every autumn and winter have brought a succession of fresh colds that have increased in severity and duration; with asthmatic features appearing first about a year ago. From age one to four years, summer, with its warmer weather, would gradually rid the child of cough and ensure it several months of freedom from acute seizures of cold. Increasingly the perennial series of winter attacks have worn the child down constitutionally, but with settled warm weather would come a prompt rebound, and through the summers the child would pick up ground lost in winter. Latterly, however, since four years of age the child has been having severe acute colds also in summer, but these are attributed by the grandmother, who would coddle the child, to overexposure brought on by swimming allowed

by the mother who had been trying to harden him.

At all times the boy has had the most approved medical attention at the hands of physicians of prominence. They have seen to it that the upper respiratory tract and its appendages have been cared for and all faults corrected. About a year ago otitis media, in severe form, appeared for the first time. This recurred, but has given no trouble since the spring of 1929. At about this time also asthmatoïd symptoms began to feature the case. There has been nothing to suggest a real or classical asthma, and any evidences of hypersensitiveness have been conspicuous by their absence. There has, again, been never any attack of typical bronchial asthma. What passes for "asthma" are attacks of wheezing, crowing and coughing, not particularly severe nor embarrassing to respiration, which are wont to come on unexpectedly. If the child is sensitive to anything it is to exposure to cold—to draughts of cold air or to stepping with bare feet on a cold floor. Such exposure will often lead immediately to coughing and wheezing. Ordinarily, the chest is clear on physical examination; and by this method alone the examining physician would pass up the child's chest as normal. Let the child step on a cold floor, and he soon begins to cough and wheeze; and now râles appear, especially in the back, to the right and at about the angle of the scapula. Ordinarily, too, he has a teasing non-productive cough that comes and goes irregularly. Seizures of apparently fresh colds, which last a few days and during which râles may or may not appear transiently in

the area mentioned, are frequent. The child's whole regimen at home has been designed to prevent these acute colds, and has resulted in a habit of life that is softening, and is, if anything, laying the boy more open to exposure.

The first suggestions of asthma sent the physician to more exhaustive search for pulmonary trouble, and in June, 1929, X-rays of the chest were taken for the first time. The search was successful. Extending out into the lung from the right hilum, in the location where râles were to be heard on occasion, was a fairly extensive opacity that was distinctly abnormal. This naturally suggested tuberculin skin testing, which resulted negatively. Accordingly, the condition was regarded as a non-tuberculous focus of infection and its exact pathological structure undetermined.

Since the child was in apparently normal constitutional health, he was allowed and encouraged to lead an active outdoor life during the early summer of 1929. In August he fell acutely ill with pulmonary and general symptoms that were immeasurably more severe than ever before. This was the onset of a serious attack of bronchopneumonia that lasted several weeks. During this illness the usual pulmonic physical signs of bronchopneumonia were confined to the right base, and X-ray disclosed a marked extension of the density noted on the earlier film. To repeat the characterization used above, the infectious focus first noticed in June seemed to have "slopped over." At any rate, there could be no doubt that here had taken place an acute exacerbation of a more

chronic sluggish process. The sequence of events was precisely that which a chronic focus of tuberculosis is accustomed to undergo, nor, during the next few weeks, did the course of the disease differ essentially from what one again and again sees in tuberculosis.

The symptoms of pneumonia subsided in good time, and with them the signs; and coincidentally also the abnormal shadow in the lung shrank to almost its former proportions. Perhaps it was a little larger than before, but within two or three weeks it was back to approximately the same size and appearance it had shown in June.

A month after recovery from pneumonia the boy arrived at the Desert Sanatorium, to enter upon treatment that was based primarily upon a climatic environment in winter that would reduce to a minimum the chances of catching fresh colds and thus flaring his chronic pulmonary process. Upon arrival he was *r*âle-free, and remained so except for occasional days on which there was always an access of cough and sometimes of wheezing. However, the child went through the winter in Southern Arizona without a seizure that could really be called a fresh cold. Except for occasional days he continued *r*âle-free, as meanwhile but little roentgenographic change appeared in his lung.

Several other patients observed during the same period have had essentially identical histories. Whatever differences stood out were merely those of detail. One or two cases had lacked the sharp and definite onset, as signalized by whooping-cough or pneumon-

ia ushering in a later childhood of "delicate constitution" and tendency to catching colds. Careful questioning of intelligent and coöperative parents made sure of this, as there emerged the story that, at one age or another during the first few years of life, a previously robust child had contracted a cold, after which a growing tendency to fresh seizures at last created a situation of settled cough, with acute exacerbations and noticeably impaired general health, always worse in the cold season and abating in summer. While all our children showed definite pulmonary change, always basal, roentgenographically its extent varied from minimal to marked. In none of this particular type were the X-ray features, symptomatology and accessory findings (for instance, finger-tips) of a kind to warrant the diagnosis of clinical bronchiectasis. Not all children had had diagnosed acute exacerbations of bronchopneumonia, and in several the probabilities of their having had it were slight.

Without exception these patients had had some special work done on nasopharynx, tonsils and adenoids, sinuses or ears, which rarely showed active trouble while under our observation. If it be assumed that these patients' oversusceptibility to colds depended on faults in the upper respiratory tract (and *adnexae*), our own patients of the type in question gradually engendered the idea that, while this may have been true originally, the cases had long passed the stage where the upper air-passages were responsible alone. At some time or other the lungs had also become affected, and rather permanently so; and it was question-

able whether at present anything but the pulmonary focus was contributing to the child's apparent defenselessness to the common cold. Indeed, little by little there developed the idea, as hazarded above, that in a great many children an abnormal tendency to the common cold is but a leading clinical expression of the presence of a non-tuberculous pulmonary focus. Perhaps the latter had originally developed in association with trouble in the upper respiratory tract. But, once created, it had become a permanent affair; and remained after upper-respiratory disturbance was allayed, and thus kept up the original complaint.

We have long learned in tuberculosis how foci of the infection, residing permanently in the lung, can be (and are) of every conceivable grade of extent and content, and therefore of clinical significance. Indeed, we have learned our lesson so well, that we teach that the presence of tubercle in the body comprehends not only foci of many kinds and sizes that are appreciable by our various modes of detection, but also a goodly array of foci that are beyond our range of observation. This fact is so easily proved as to constitute one of the important truths of tuberculosis. In other words, a complete understanding of the habits of the infection, tuberculosis, must always postulate that for every focus of demonstrable tubercle there likewise exists an unknown ratio of hidden tubercles, which, for one reason and another, do not disturb function or stand out morphologically sufficiently to make their presence noticeable.

Can the case be similar with these non-tuberculous infectious foci that we have been discussing? We cannot answer with the positive evidence from experience with the child, but we may cite a bit or two of testimony that points to the high probability of the case in question.

For instance, how are we to explain what can be found to happen not rarely in adults, and quite likely also in children, had we the proper opportunities to follow them medically? Instances, such as I am about to enlarge upon, are peculiarly the opportunities of the family physician to whom it is given to observe under many circumstances the same individual patient through the years.

The opportunity will begin, let us say, with a severe common cold. The patient takes to bed with the usual symptoms, including a fever of a few degrees, and the examining physician detects basal râles. Within three or four days the patient makes an ordinary recovery, as the temperature falls to normal; and he prepares to get up and be about his daily work, feeling a little bit shaky perhaps, yet as well as can reasonably be expected immediately after a hard cold. But now the physician is disturbed to find that, though clinical symptoms are about over with, the base still shows râles. Justly concerned, he counsels the patient's remaining in bed. Fearful of pneumonia, he plans to keep the patient there until the râles have disappeared.

By the end of another week we have a patient who is feeling better every day and impatient to be up and about his daily round, yet displaying a lo-

calized patch of râles that is hardly less noticeable than during his acute illness. There may be a little cough, and perhaps scanty expectoration; but otherwise the patient is thoroughly asymptomatic, and to all intents and purposes he has recovered completely. Only by virtue of the râles can he be regarded as ill and still requiring fairly rigorous treatment.

Patients of this type present a pretty problem to the responsible physician who attends them for the first time. If he decides to "wait out" the râles before allowing the patient up, he may wait for months, especially if it is winter. Frequently such râles do not disappear promptly. Indeed, they do not fade out completely for months. In not a few patients they will persist until the warm and settled weather of summer, when gradually they die away. Call this condition what you will—pneumonitis, subacute or subchronic, or with delayed resolution, or minimal pneumonia of kindred types, or localized bronchitis—we really don't know a thing about its pathological nature, its structure.

But it is the patient who, as it happens, begins to repeat this experience, that becomes the really interesting subject for speculation. It may be the next winter, it may not be until several years later, that the physician is called to attend the same patient with another hard cold. There is the same lot of symptoms, with fever again uppermost for two or three days, after which ensues the same prompt clinical recovery as before. Again, too, there are basal râles, which once more do not subside with the other features of the infection. It is not particularly

noteworthy that a patient has contracted a second common cold, for this is the archetype among the habitually recurring infections of mankind. But what is likely to bid the physician pause and reflect is the circumstance that he again finds râles, and again persistent râles, in the very same spot that yielded them before and which, to his knowledge, had been entirely quiet during the intervening year or two. This surely is curious: that two separate attacks of the common cold picked up afresh from the outside at an interval of several years, should focalize in the same sound lungs at the same place.

The case becomes still more curious when, as occasionally happens, a patient will go through this performance, not once or twice, but repeatedly through the years: when every recurrent acute cold will make for focal râles located always in the same region, which, in the intervals between attacks, will be found to be not only râle-free but also normal to ordinary methods of physical examination.

Nevertheless, it is possible that, the more frequently this experience is repeated in the individual patient, the less curious it becomes and the more certainly we are approaching a satisfactory explanation. Every recurring episode of this kind enlarges the probability that these patients have actually a permanent infectious focus within their lung, minimal perhaps and undetectable in ordinary normal times by the methods used, yet, like foci of tubercle again, capable of exacerbation under the influence of intercurrent infection (for instance, the common cold), when now they suddenly

flare to proportions recognizable by our methods of diagnosis.

A recent patient furnishes a beautiful example of perhaps a later phase of this condition: Fifty-three years old now, he began at thirty-seven with a severe cold to enter upon a series of recurring colds and, later, attacks of bronchopneumonia that succeeded one another, always in winter through the years between. Always were the changes focal and localized in the same place, the left base. After some years the changes were of a grade and kind that shadowed the X-ray film, and during the past few years, that have been featured by several pneumonic seizures, the morbid markings on the films have extended. Latterly an excavation (abscess) has come into view in the centre of the affected territory. For some years there have been increasing asthmatoïd symptoms, whose onset was not until years after the beginning of the pulmonary process and which respond with notable delicacy to exposure to cold. Almost twenty years of repeated reactivations of this non-tuberculous focus have left their mark upon his heart, which for the first time displayed serious embarrassment last winter during the most severe attack of bronchopneumonia yet experienced. The case is an almost perfect example of the slow yet orderly march of a non-tuberculous focus from small and merely symptomatic beginnings to extensive pathological change. We have here a march that at present we may be allowed to imagine something as follows: With or without morbid changes in the upper respiratory tract, microorganisms other than tubercle bacilli gain access to the lungs, take

hold, and focalize, preponderantly out from the hilum and below midlung. Tissue changes may be so minimal as to escape detection and recognition by any present diagnostic method: it is conceivable that ordinary autopsy would miss them, as, too, would histological examination short of complete serial sectioning. Like the gonococcus in the prostate or the posterior urethra, the *Bacillus typhosus* in the gall-bladder, the *Bacillus diphtheriae* in the tonsil, the *Bacillus tuberculosis* anywhere, the germs can live on indefinitely, embedded in minimal focal lesions, and multiplying sparsely. Like the focus of tuberculosis, this non-tuberculous focus is capable of indefinite activation, especially by other intercurrent respiratory infections. In its lowest clinical phases it throws out clinical symptoms and signs only when thus activated, and its earliest detectable phases are these periods of audible focal râles, noticeable during activation and often long afterward, and at a stage too poorly developed anatomically to show pathologically on X-ray. At this time and during periods of focal quiescence, the lung will appear normal on physical examination.

Because symptomatology that suggests an oversusceptibility to colds is a prominent feature of cases with demonstrable non-tuberculous focal infection, a marked tendency to colds in children, especially if not satisfactorily accounted for, should indicate a most exhaustive search for pulmonic focal infection. In the absence of all other signs, râles recurring in the same place are first-class evidence of its presence. Because of the incurability of later phases it is important to institute treat-

ment at this earliest presumptive indication of its presence.

With a later and more definite pathological development the tissue changes set up by these focal infections begin to cast abnormal markings on the X-ray film. It may take years to reach this stage, though in many children the time is much shorter. What is important is to appreciate that, for purposes of treatment, this is a comparatively advanced stage and that the ideal is to anticipate it with treatment. The chances for acute episodes of bronchopneumonia are now multiplied—attacks which, in their turn, enhance the progressiveness of the focus. This is the stage that will be found in many children whose leading complaint is oversusceptibility to colds, and every effort should be made to detect it in the circumstances. It is also a stage that is often featured by symptoms that suggest asthma, though the symptoms are likely to lack the leading features of those of the classical disease.

Firmly entrenched, these focal infections can progress to bronchiectasis and to abscess, as, too, the tendency to

recurrent bronchopneumonia may become more marked, and that to contracting fresh colds enhanced, and the child shows more decided constitutional effects. At this stage the interminable succession of alleged fresh colds is more likely to be the more frequent acute manifestations of the chronic focus, now more or less active clinically all the time. Attempts to eradicate such foci will be rarely successful; treatment may palliate; it can hardly obliterate.

In view of our present therapeutic resources (or lack of them) the guiding principle of treatment of the minimal processes will be that regimen in that environment that reduces to a minimum the chances of catching fresh colds or of acutely exacerbating the focus. The standard winter climate is the dangerous element for these patients. They do badly, and repeated activations wipe out all possibilities of healing. At present there is reason to believe that, if taken in hand early enough and if allowed long enough periods of quiescence, many of these foci may attain permanent arrest and healing.

The Effect of Sodium Malate Combinations Upon Gastric Acidity

By JOHN C. KRANTZ, JR., Ph.D. AND A. A. SILVER, M.D., *with the technical assistance of* BERNARD J. HOFFMAN, *Baltimore, Md.*

IN a previous communication to this journal, one of us (J.K.) (1) studied the metabolism of a certain sodium malate mixture when employed as a dietary substitute for sodium chloride. The mixture studied consisted of 85.5 per cent of disodium malate, 9 per cent of trisodium citrate, 5 per cent of triammonium citrate and 0.5 per cent of manganese bromide. In this work the administration of this mixture of salts in the form of a condiment was shown to influence the acid-base equilibrium of the urine in the direction of the alkaline side. The malic acid was apparently completely metabolized.

A physician friend of one of us (J. K.) whose stomach acidity was abnormally high and who suffered with the usual symptoms was brought to the attention of the authors. It was suggested as an experimental measure that he eliminate the use of sodium chloride as a condiment from the diet and replace it with the sodium malate mixture. After three months use of this material, the patient reported greatly relieved symptoms and a more liberal protein diet. He reacted favorably to the use of the condiment. On account of this, the authors began a system-

atic investigation of the action of the sodium malate mixture upon gastric acidity.

EXPERIMENTAL

An artificial stomach contents was prepared according to the following formula²:

Hydrochloric Acid	sufficient to make	1/40 per cent
Lactic Acid	sufficient to make	1/80 per cent
Butyric Acid	" " "	1/100 per cent
Acetic Acid	" " "	1/100 per cent
Pepsin, U.S.P.	2.0 Gm.
Rennin, N.F.	1.0 Gm.
Sodium Chloride	0.1 Gm.
Disodium Phosphate	0.1 Gm.
Albumin	0.2 Gm.
Glucose	0.1 Gm.
Water	sufficient to make	1000 cc.

This mixture was divided into 25 cc. portions and different quantities of sodium malate mixture added to each portion. The total acidity was determined by titration using phenolphthalein as an indicator in the usual manner. The hydrogen-ion concentration was determined electrometrically using a Wilson³ type hydrogen electrode. The results obtained are given in Table I.

Another sample of artificial gastric contents was prepared increasing the

TABLE I

No.	Gm. Sod. Malate Mixture in 25 cc.	pH	Degrees Acidity cc. 0.1 N. NaOH to titrate 100 cc.
1	none	1.38	95
2	0.25	2.92	95
3	0.50	4.07	100
4	0.75	4.43	103
5	1.00	4.64	108
6	1.50	4.89	110
7	2.00	4.97	117
8	2.50	5.10	121
9	3.00	5.17	125
10	3.50	5.22	128
11	4.00	5.25	137
12	6.00	5.39	155

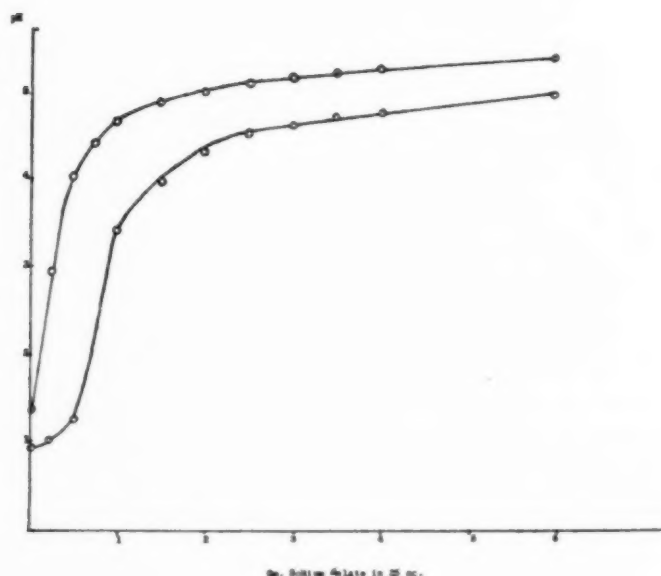
TABLE II

No.	Gm. Sod. Malate Mixture in 25 cc.	pH	Degrees Acidity cc. 0.1 N. NaOH to titrate 100 cc.
1	none	0.95	242
2	0.25	1.05	242
3	0.50	1.28	242
4	0.75	2.61	242
5	1.00	3.40	248
6	1.50	3.97	251
7	2.00	4.32	255
8	2.50	4.51	260
9	3.00	4.61	272
10	3.50	4.70	275
11	4.00	4.76	278
12	6.00	4.90	281

quantities of the four acids employed in the formula four fold. This more acidic mixture was subjected to the same procedure as the preceding one. The results are recorded in Table II.

The influence of sodium malate mixture upon the hydrogen-ion concentration of the gastric contents of the two different degrees of acidity can be readily observed from Graph No. I.

GRAPH NO. I



These experiments on artificial stomach contents indicate that the sodium malate mixture has a definite influence in reducing the hydrogen-ion concentration of the fluid. There is also observed a gradual increase in the total acidity. This we found to be due to some free malic acid in the sodium malate mixture which requires additional alkali for neutralization.

Having ascertained the influence of the sodium malate mixture upon artificial stomach contents, the procedure followed next was to determine its influence upon gastric acidity *in vivo*.

Nine individuals, whose history as far as gastric disturbances is concerned was negative, were given a test meal after a twelve-hour period of fasting. The meal consisted of two slices of wheat bread without crust and 500 cc. of water. Forty minutes after the ingestion of the meal the stomach contents were removed by intubation and the hydrogen-ion concentration and total acidity determined as previously described. Table III records these results.

TABLE III

Individual	pH stomach contents	Degrees Acidity cc. 0.1 N. NaOH to titrate 100 cc.
J.	1.86	17
Fr.	1.55	38
K.	1.77	31
M.	1.30	66
Jo.	1.65	40
B.	1.83	40
C.	1.31	75
H.	1.92	19
W.	1.87	24
Mean	1.67	Mean 39

We considered the contents of the nine stomachs normal in view of the comprehensive work of Shohl and

King⁴ in the Brady Institute of the Johns Hopkins Hospital. These investigators observed the limits of peptic digestion to be within the pH range 1.3 to 4.0 with an optimum at pH 1.65. On the following day seven of the nine individuals returned for a second intubation. The test meal administered this time was identical with that formerly given with the addition of six grams of the sodium malate mixture dissolved in the water. Under the same experimental conditions the results tabulated in Table IV were obtained.

TABLE IV

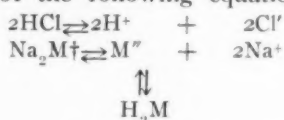
Individual	pH stomach contents	Degrees Acidity cc. 0.1 N. NaOH to titrate 100 cc.
J.	4.20	31
K.	4.40	38
Jo.	4.08	33
B.	3.91	33
C.	4.06	38
H.	2.63	47
W.	3.11	66
Mean	3.77	Mean 41

DISCUSSION OF RESULTS

From the experiments upon the artificial stomach contents, it is evident that the sodium malate mixture buffers the hydrochloric acid of the gastric contents. Furthermore, with as small a quantity as 0.25 gm. of the mixture the pH (Table I) was changed from 1.38 to 2.92. It should be emphasized at this point that such a change in pH on the extreme acid range of the scale is very significant. Bearing in mind that pH is a logarithmic value, Gortner⁵ has made the following interesting comparison. If the various points on the pH scale are

compared with cubical containers varying in size in similar numerical ratios, a pH change from 6 to 7 would be represented by a cube having an edge of $\frac{1}{4}$ inch, whereas within the region of extreme acidity, say 1 to 2, would be represented by a cube with an edge $11 \frac{9}{32}$ inches.

The mechanism of the change in pH when sodium malate mixture is added can be readily understood by a study of the following equation:



When sodium malate is added, the foregoing equilibrium is established. The reaction proceeds in the direction of free malic acid for it is the least ionized product. Thus theoretically the total acidity (with phenolphthalein as an indicator) will remain constant but the hydrogen-ion concentration will diminish upon the addition of sodium malate to gastric contents. Although Rehfuess⁶ has pointed out, after a study of 800 gastric contents, that there is no degree of acidity found in disease that cannot be encountered in health, it is conceded that the determination of the hydrogen-ion concentration is probably the most significant measure of gastric acidity in suspected pathological conditions.

In the normal stomach contents examined (Table III) the probable error of the pH determinations calculated by the simplified formula

$$\text{P.E.} = 0.8453 \frac{\sum D}{N}$$

is 0.16 unit pH. A difference to be

[†]Where M represents the malic acid radical.

significant must be at least three times the probable error or a difference of 0.48 pH unit. The mean of the pH of the stomach contents of the seven individuals after receiving the sodium malate mixture was 2.10 units pH higher. Therefore, the difference can be attributed to the influence of the sodium malate mixture. It is interesting to note that the means of the total acidities are not significantly different. This is what one might expect from the foregoing mechanism of buffering. This is dissimilar to the addition of a free base to the acid where actual neutralization would occur removing the hydrogen ions from solution by union with the hydroxyl ions of the base forming very slightly dissociated water. In the latter case a decrease of hydrogen-ion concentration would result also in a decrease in total titratable acidity. As the mechanism of the buffering action of this substance is different from the neutralization of the acid by free bases, carbonates or bicarbonates, it is possible that its use in the treatment of hyperacidity may not be accompanied by a subsequent increased secretion of hydrochloric acid as experienced when the ordinary alkalies are administered. Although 6 gm. of the sodium malate mixture was administered to obtain the change in pH of two units, the authors attach much significance to the fact that with the artificially prepared gastric contents where natural variations in acidity and psychic factors are eliminated, a very small quantity of the sodium malate mixture produced a marked therapeutic change in hydrogen-ion concentration.

Shohl and King⁴ in their investigations emphasize the significance of the

determination of the buffer value of gastric contents. They define the buffer value as the amount of acid or alkali necessary to be added to bring about a definite change in reaction. More recently Van Slyke⁷ has comprehensively studied the capacity of buffer substances and by methods which were unequivocal arrived at a measure of the buffer capacity of solutions. The unit proposed by this

worker is the differential ratio $\frac{dB}{dpH}$ which expresses the relationship between the increment in gram equivalents per liter of a strong base B added to a buffer solution and the resultant increment in pH. Using the measurable increments $\frac{\Delta B}{\Delta pH}$ as sug-

gested by Van Slyke and used by one of us in other investigations (8, 9, 10) an average approximation of the buffer capacities of the gastric contents of these individuals without and with the sodium malate mixture can be determined.

In the titration of acidity with alkali hydroxide the faint pink color of the indicator phenolphthalein appears at pH 8.3. Let us assume that each titration was carried to this hydrogen-ion concentration. The average amount of tenth-normal sodium hydroxide required to change the pH from 1.67 to 8.3 is 390 cc. per liter or 0.039 mole sodium hydroxide, therefore:

$$\frac{\Delta B}{\Delta pH} = \frac{0.039}{6.63} = 0.0059$$

After the ingestion of the sodium malate mixture, 410 cc. was the average

quantity of tenth-normal sodium hydroxide required to change the reaction from the average pH 3.77 to pH 8.3. Similarly this may be represented:

$$\frac{\Delta B}{\Delta pH} = \frac{0.041}{4.53} = 0.0091$$

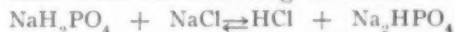
It is obvious that the buffer capacity of the gastric contents is increased by the addition of sodium malate mixture. We wish to emphasize that the buffer capacity is different at different points on the pH scale and these measurements serve only as comparisons. The evidence of the varying buffer capacity of the gastric contents may be ascertained by a study of the slope of the curves in Graph I.

SUMMARY

1. A study of the action of sodium malate mixture upon gastric acidity has been made in vitro and in vivo.

2. This substance possesses the capacity to reduce the hydrogen-ion concentration of gastric acidity and hence the opportunity for its use in hyperacidity is made available.

3. According to the theory of Maly¹¹ gastric hydrochloric acid results from the following reaction.



If we accept this theory as correct the use of this sodium malate mixture as a condiment in cases of hyperacidity to replace table salt would seem to possess a two-fold advantage; first, the decreasing of the free gastric acidity and second, the elimination of a potential source of hydrochloric acid.

BIBLIOGRAPHY

- ¹KRANTZ, JOHN C., JR.: *Ann. Int. Med.*, 3 (1930): 826.
- ²WEBSTER AND KOCH: *Manual Physiol. Chem.*, University Press, Chicago.
- ³WILSON, J.: *Ind. and Eng. Chem.* 17 (1925): 74.
- ⁴SHOHL, A. T. AND KING, J. H.: *Bull. Johns Hopkins Hosp.* 31 (1920): 158.
- ⁵GORTNER, R. A.: *Outlines of Biochemistry*, Wiley and Sons, New York, 1929, p. 93.
- ⁶REHFUSS, M. E.: *J. Am. Med. Ass'n.*, 71 (1918): 1534.
- ⁷VAN SLYKE, D. D.: *J. Biol. Chem.*, 52 (1922): 525.
- ⁸KRANTZ, J. C., JR.: *J. Am. Pharm. Ass'n.* 18 (1929): 469.
- ⁹KRANTZ, J. C., JR.: *J. Am. Pharm. Ass'n.* 19 (1930): 366.
- ¹⁰KRANTZ, J. C., JR. AND CARR, C. J.: *J. Phys. Chem.* 35 (1931): 756.
- ¹¹MALY'S JAHRESBERICHT, APPLIED BIO-CHEM., MORSE.: Saunders & Co., Philadelphia, 1927, p. 433.

Tuberculin Therapy

By MILES J. BREUER, M.D., F.A.C.P., *Lincoln, Nebraska*

THE controversy over the efficacy of protein extracts of tubercle bacilli in the treatment of tuberculous patients, has seemed somewhat puzzling, and without solid ground to rest upon. Successful results are ardently claimed by some, and denied with equal emphasis by others. Usually this sort of a situation means that no rational basis has as yet been arrived at for the application of the treatment.

It is only very recently that we have acquired accurate knowledge of the principles underlying the reaction of the animal body to tubercle bacilli and tuberculo-protein. However, at present we have a sufficiently comprehensive conception of tuberculous allergy and tuberculous immunity to enable us to formulate at least a tentative working basis for the scientific use of tuberculin in therapy. Any such therapy must naturally be based upon and in accord with the facts of allergy and immunity as they have been learned from animal experimentation and pathological study, and with the principles that have been deduced therefrom. Therefore, a brief inquiry into these facts and principles is advisable in this place.

Immunity is that characteristic of the tissues by virtue of which tubercle bacilli are not able to survive there. A subject with good immunity survives infection with tubercle bacilli, whereas

one with low immunity dies quickly from the effects of such infection. The prompt death of non-immune animals does not at all involve the extensive presence of the well-known anatomical pathology of tuberculosis. Death takes place in a non-immune animal in the total absence of visible pathological lesions. Such lesions are due on the one hand to the allergic reaction to the tuberculo-protein, and on the other, to the foreign-body reaction of the tissues to the lipoid capsule of the tubercle bacilli.

Allergy is a sensitization of the subject's tissues to initial inoculation of tuberculo-protein, by virtue of which subsequent inoculations produce inflammation in these tissues. A first dose in a non-allergic animal, whether it be an injection from a needle or a natural infection, produces no observable effects; no inflammation, no symptoms, no visible lesions. But an effect has been produced nevertheless, for a second dose will produce all the well-known local and systemic inflammatory phenomena: hyperemia, exudate, fibrosis, or necrosis; fever, malaise, anorexia, nutritional disturbances. The nature and severity of the symptoms will depend on the degree of sensitization that has been established, and the size of the subsequent doses. The initial dose has in some way sensitized the body cells¹ so that they respond to

subsequent doses with the phenomena of inflammation. This sensitization is probably due to the development of antibodies which split the tuberculo-protein into toxic substances; but on that matter, knowledge is not as yet accurate.

A subject rendered allergic by initial inoculation, is also rendered to a greater or less degree immune. It will survive a larger dose of tubercle bacilli than it could have survived previous to the initial injection. Yet, immunity and allergy are not the same thing. They do not even run parallel, but are totally independent of each other. It merely happens that in many cases they are associated.

For example, if a subject is made allergic by inoculation with living tubercle bacilli, it will develop a much higher degree of immunity (survival ability) than if inoculated with dead bacilli or with tuberculo-protein. Dead bacilli do produce some degree of immunity, but from a practical therapeutic-value standpoint, only an insignificant one. Yet, the degree of allergy developed in either case, whether living or dead bacilli are injected, is precisely the same. It depends only on the amount of tuberculo-protein injected and on nothing else.

A high degree of allergy may exist in a subject that has little or no immunity. Infants infected with massive doses, or the tuberculosis of savages coming into city surroundings, are an example of this state of affairs. There is high fever, severe illness, extensive inflammatory pathology with exudation and necrosis, rapid course, and early death.

Conversely, we may have a low degree of allergy existing coincidentally with a high state of immunity. Willis² showed that guinea pigs after a lapse of two and a half years following an immunizing inoculation with tubercle bacilli, had practically lost all their allergic sensitiveness, but were still as highly immune as were the allergic control animals. Clinically, individuals are not uncommonly found harboring tuberculous pathology of considerable extent without any allergic symptoms, yet with sufficient immunity to continue to survive without suffering harm, and without even being conscious of their pathology.

Allergy and immunity may both be absent in an individual at the same time, as in the case of a guinea-pig that has been kept away from contact with tubercle bacilli. A dose of sufficient size will kill it promptly without any inflammatory reaction whatever. The two states may be developed to a high degree in the same individual, as in the commonly found clinical cases in which the patient is severely ill, with numerous inflammatory symptoms, and yet survives and eventually achieves a high degree of recovery.

Tuberculin, which is the protein extracted from the bodies of tubercle bacilli, has exactly the same effect on injection as do the dead bacilli, with the exception that the tubercle-forming reaction due to the presence of the lipoid capsule is lacking. The effect of its injection into the animal body is, initially, to produce the allergic state. Subsequently, the injection of a large dose will produce a severe reaction, with inflammation, exudation, and necrosis. But, a series of smaller

doses, properly graduated and timed will de-sensitize the individual and diminish the allergic state, so that larger and larger amounts of tuberculo-protein can then be administered without systemic or local disturbance.

It was stated above that the injection of tuberculo-protein has on *immunity* only a negligible effect. There is some disagreement among workers in this field as to whether it will produce any immunity at all. Krause denies it³, whereas Petroff and Stewart⁴ find that some degree of immunity is produced, but agree that it is very slight indeed; certainly not of sufficient importance to be a consideration in clinical therapeutics.

Therefore, if tuberculin is to be used clinically, in the treatment of tuberculous patients, it cannot be for any effects that it may have in increasing immunity. It will do little or nothing to prevent the bacilli from killing the patient; it will not prevent reinfection or additional infection. It can only be used to reduce allergic sensitization.

Allergy, however, is at the bottom of a large proportion of the patient's illness and clinical symptoms, of his distress and discomfort. His fever, his malaise and reduction of capacity for effort, his lack of appetite and loss of weight, are all allergic phenomena. Allergy is responsible for the inflammatory process with its exudation and its necrosis. The whole "toxic" and inflammatory picture is due to allergy. It is completely absent in non-allergic animals dying from lethal doses of tubercle bacilli.

It would be of immense value to the tuberculous patient if he could by some means be relieved of this burden of

distress and this load of inflammation. Even though such means might possibly not be curative, nor life-saving, nevertheless it would be of distinct benefit. The patient could be made comfortable and useful. The relief of distressing symptoms is equivalent to reduction of stress for the patient, and reduction of stress is one of the chief considerations in the treatment of the tuberculous patient, and one of the greatest contributions toward recovery.

A priori, therefore, tuberculin should be indicated in those cases whose symptoms are chiefly of allergic origin; i.e., those which are inflammatory in character, or connected directly or indirectly with inflammatory processes.

In selecting cases for such treatment, the distinction must be observed between symptoms of allergic origin, as already enumerated, and those of reflex origin. Pains and functional disturbances in the viscera, the heart, larynx, stomach, large and small intestine, uterus, could hardly be expected to receive direct benefit from tuberculin treatment. These symptoms are of neurological nature, due to the existence of definitely established abnormal paths for nervous impulses. It is necessary to recognize their essential difference from allergic symptoms in selecting cases for tuberculin treatment. Yet, as their source is originally a localized inflammation that has set up the irritation within the nervous system, ultimately the control of the inflammation ought to furnish the hope of relief even for the abnormally functioning reflexes.

About a year has passed since these ideas were definitely crystallized. Dur-

ing that year the writer has had the opportunity of selecting twenty-six appropriate cases, and studying the effect of tuberculin treatment with this idea in mind. The following observations were made:

The cases were all controlled cases, as they had previously failed to respond noticeably to general therapeutic regimen. None of them were severe nor advanced cases. Treatment was in each case begun with 0.00075 mgm. of Mulford's Old Tuberculin, and continued empirically, the size and frequency of dosage being determined by the patient's reactions and his increase in tolerance.

- 14 cases clinical symptomatology purely allergic.
- 11 cases mixed with reflex symptomatology reflex in minority.
- 2 cases unable to obtain any desensitization; unable to increase dosage or to continue treatment. Reason unknown.
- 4 cases impossible to obtain sufficient control over patient's behavior to render observation of any value; the unknown amounts of tuberculin liberated by excessive physical activity obscured results.
- 20 cases tolerance to tuberculin raised so that within 2 to 5 months, 15 mgm. of tuberculin could be injected without more than moderate reaction.
- 4 cases original temperature of patient remained unchanged in spite of increased tolerance to tuberculin.
- 6 cases temperature reduced to normal.
- 11 cases temperature lowered by 1 degree or more, though not brought to normal.
- 16 cases gain of 5 percent or more in weight
- 4 cases gain to standard weight.
- 16 cases distinct decrease in malaise and fatigue; improvement in physical state.

8 cases reduction of pulse rate from near 100 to near 80.

5 cases change for the better in local physical findings: râles, respiratory movements, nutritional state of shoulder-girdle muscles, localized density, etc.

5 cases (out of a total of only 6 who were checked two or more times by X-ray) definite change toward the fibrosed type of X-ray shadow.

19 cases one or more signs or symptoms of improvement.

6 cases improved condition maintained for 6 months without further tuberculin treatment, but with adequate hygienic precautions.

At first glance, the amount of improvement obtained may not seem anything revolutionary, or vastly different from previously reported figures. But when the fact is taken into consideration that these are thoroughly controlled cases, which previously failed under all other efforts, and which improved under no other additional method than the tuberculin, and that they were selected for their allergic symptomatology, the results are suggestive.

I have been able to go back over my records for nearly ten years, and make an accurate analysis of tuberculin therapy instituted during that period. This was the period during which I have been using a standardized record-form for recording history, examination and treatment². During this period I find 181 cases treated with tuberculin. Seventy-nine of these showed improvement attributable to tuberculin; and of this 79, 41 showed very satisfactory results or arrest. The significance of this 22 per cent of satisfactory results among improved cases, is modified by two factors: approxi-

mately 50 per cent of the 181 cases were only slightly or moderately advanced, since during this period we have been trying to make a point of early diagnosis; secondly, in addition to tuberculin treatment, every other possible therapeutic means was used. This of course increases the significance of the figures in the previous group, which were selected as not having responded to general treatment.

In all of these 79 cases, allergic symptoms were a prominent feature:

Fever of 100 or more	79
Subnormal weight	74
Anorexia	77
Râles	64
Localized density	48
Exudative X-ray shadow	21
Reduced effort capacity	78
Tachycardia	70
Headache	27
Malaise	74

In the 102 cases in which the results of tuberculin treatment were unsuccessful or unsatisfactory, the signs and symptoms of the visceral-reflex type predominated:

G-I symptoms, irritative type	69
G-I symptoms, atonic type	12
Asthma	4
Chest, back, and arm pains	60
Vague abdominal pains	22
Pains in occiput and neck	46
Menstrual colic	4
Bradycardia	4
High nervous drive (low basal rate)	12
X-ray shadow limited to fibrosis	21

The two groups of cases compare as follows:

Improvement noted:

43.6 percent in unselected, uncontrolled cases

76.0 percent in allergically selected, controlled cases

In this latter group, 16 percent failed to receive benefit from tuberculin because of environmental factors, and only 8 percent because of failure of the tuberculin to work properly.

This report is preliminary and can only be suggestive. Further observation on a larger number of cases is required to test the validity of the theoretical considerations, and to develop skill in handling various phases of the therapeutic method, such as selection of cases, graduation of dosage, etc.

SUMMARY

1. The effect of tuberculin is to decrease the patient's allergic sensitization.
2. Its effect in increasing immunity is negligible.
3. Clinically it ought to be useful in those cases in which the allergic state is principally at the basis of the patient's symptomatology.
4. A series of 26 previously unresponsive cases selected for treatment with this distinction in view, showed no contradiction and probable confirmation of the above idea.
5. Analysis of 181 unselected cases previously treated, also confirms the idea.

REFERENCES

- ¹RICH AND MCCORDOCK: An Enquiry Concerning the Role of Allergy, Immunity, and Other Factors of Importance in the Pathogenesis of Human Tuberculosis, Bulletin of the Johns Hopkins Hospital, XLIV, No. 5, pp. 273, 424, May, 1929; page 307.
- ²WILLIS: Am. Rev. of Tuberc. 1928, XVII, p. 240.
- ³KRAUSE: Am. Rev. of Tuberc. 1917, 165.
- ⁴PETROFF AND STEWARD: Jour. Immunol. 1926, XII, 97.
- ⁵BREUER: Ann. Int. Med., III, Jul. 1929, p. 57.

Present Status of Heliotherapy in Tuberculosis*

By CHARLES K. PETTER, M.D., *Glen Lake Sanatorium, Oak Terrace, Minnesota*

*"'Let there be light,' said God; and forthwith light
Ethereal first of things, quintessence pure
Sprung from the deep."*

MILTON'S quotation exemplifies the aphorism that light is life. Metabolism and the vital processes of higher organisms are impossible, while our material universe could not have developed, without light. Every race of man has looked upon the sun as a god of comfort, health and life. Little wonder is it then that the earliest written histories of the Egyptian, Babylonian, Iranio-Persian, Greek, Roman and Hebrew peoples refer to the sun first as a source of light, then as the deity of health and life. (Aton, Baal, Mithra, Apollo and Helios are the names given these various deities.)

Coming on down through the ages we find discussion of heliotherapy procedures by such men as Herodotus, Hippocrates, Celsus, Galen and Cicero. In the middle ages Avicenna recommended sunbaths for his patients while Paracelsus first recommended mountain climate as most suitable for sun cure.

Nothing much further appears until an awakening of interest in helio-

therapy took place on the part of the French, when Rousseau called attention to the potentialities of sunlight in 1735. In 1815 Cauvir published a paper in which he says, "Speaking of scrofulous infants, send them to the country, feed them up as well as possible, but above all, make them roast, burn and roast in the sun." Ollier and Poncet of Lyons treated tuberculous arthritis by sunlight in 1840.

The further development of modern heliotherapy has taken place particularly through the efforts of Bernard, Rollier and Finsen. Finsen was the pioneer in artificial heliotherapy while as Guavain says, "Rollier is the 'High Priest' of modern sun worship; he has led us back to sunshine and simplicity, to the first principles of light and life."

One cannot discuss heliotherapy without at least a brief consideration of the physics involved. Light has been defined as "an electromagnetic disturbance of the ether." (Lodge) The electromagnetic vibrations which pervade our universe when arranged according to wavelengths present a definite spectrum. At one extreme the waves are measured in ten millionths of a millimeter while at the other end

*Read before the Meeting of the Resident and Consulting Staff Glen Lake Sanatorium, Oak Terrace, Minnesota. November 19, 1930.

of the spectrum hundreds of meters express the wave lengths. (Figure 1.)

In addition to wave length, these ethereal agitations possess a velocity of 186,300 miles per second and a frequency varying inversely as the wave length. This entire electromagnetic spectrum if projected as one view, with the visible part one foot in length, would be seven million miles long. At one end are the recently observed cosmic rays and at the other the Hertzian or radio waves, with gamma and X-rays, ultra-violet, visible light, and penetrating heat or infra-red rays in between. (The Angstrom unit, one ten millionth part of a millimeter, has been accepted as the unit of measurement.)

We are particularly interested in a combination of the near ultra-violet

and the visible spectrum in treating tuberculosis.

Although many people believe the beneficial effects of heliotherapy due to the ultra-violet component, I believe that conclusive evidence has been presented by many observers to show that wave lengths of 3900 to 8000 \AA (visible) are a necessary adjunct to the biotic or vital rays, (2800-3800 \AA); in other words, a spectral range from 2800 to 8000 \AA whether from the sun direct or from an artificial source (carbon arc) is the agent of choice.

Radiant energy in the range mentioned (2800-8000 \AA) produces very definite physiologic effects, some due to the ultra-violet alone; others to the visible alone and still others to the entire range. These effects are briefly:

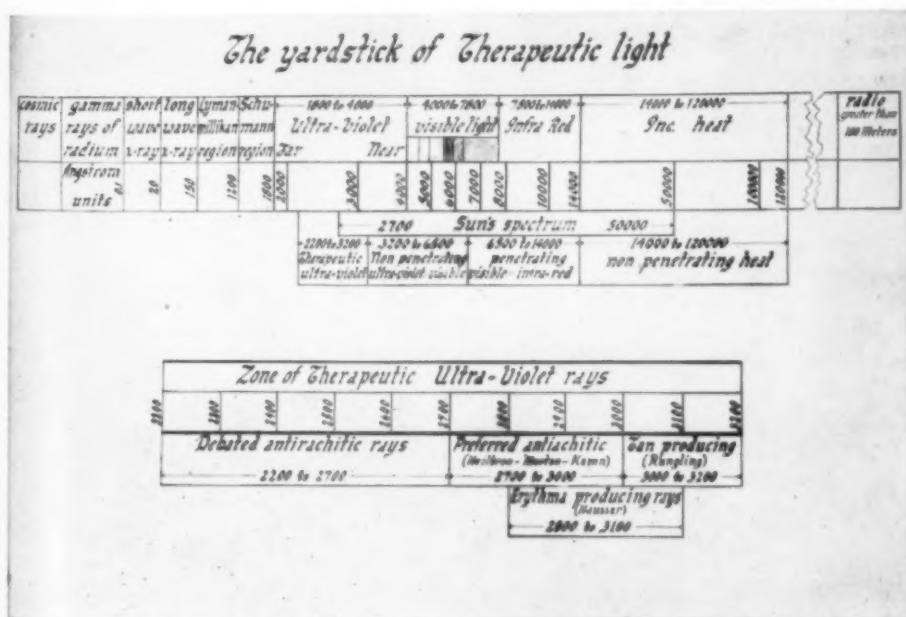


FIG. 1. Diagrammatic representation of electromagnetic spectrum, showing wave lengths in Angstrom Units.

1. Erythema and slight tanning accompanied by improvement in the health, texture and function of the skin.

2. In the blood there is an increase in hemoglobin, a rise in red count and platelet count. The lymphocytes show an initial drop following irradiation with subsequent rise while the polynuclear elements are increased.

3. The calcium phosphorus balance is brought to normal.

4. Blood pressure tends to become lower, while pulse rate shows an initial rise with subsequent drop to normal or below.

5. Body temperature experiences an initial rise but returns to within one degree of normal shortly after irradiation has ceased.

6. Basal metabolic rate is not increased but elimination is aided. Blood urea nitrogen is reduced and nutrition improved.

7. Muscles experience an improvement in tone, contour and nutrition. Rollier has referred to sun bathing as the best masseur one can employ.

8. Healing is stimulated and tuberculous processes affected quite specifically.

9. There is probably a definite chemical effect on the blood, the rays penetrating to the capillaries where their energy is absorbed by the blood stream and effects produced on distant tissues and organs.

10. Sunbaths produce the liberation of varying amounts of tuberculin and thus act the same as work on the tuberculous process. Graduated doses of light liberate controllable amounts of tuberculin while physical activities may produce more than is desired.

The present day popularity of both natural and artificial irradiation as a beneficial measure has led to much injudicious use of this therapeutic agent. Edgar Mayer has stated in this connection, "Light of any form by itself is not curative, but comprises only one of the important adjuncts in the treatment of tuberculosis. To believe that sunlight or artificial sources of light will cure all forms of surgical tuberculosis, to be unduly optimistic about this treatment and to consider it a specific form of treatment, to use it without sound medical guidance and adequate equipment, and finally to employ it to the exclusion of rest and hygienic regimen, eliminating orthopedic measures or the occasional necessary surgical intervention in bone and joint tuberculosis is bound eventually to dishearten many sufferers and to bring discredit on an otherwise desirable method of treatment."

Let us then be a bit conservative in our properly enthusiastic application of heliotherapy in tuberculosis.

If we follow the plan outlined by Watson (figure 2) untoward results will be avoided and a rational system of heliotherapy carried out.

The child with tracheo-bronchial glandular tuberculosis presents a very definite indication for heliotherapy and the treatment will give him the maximum insurance against future disability from tuberculous disease.

In the treatment of the adult form of pulmonary tuberculosis with heliotherapy, much unnecessary fear and unjust criticism of this therapeutic agent has arisen. True, every case of pulmonary tuberculosis cannot be given sunbaths; in fact, only a minority of

these patients can be so treated. Yet hemoptysis, miliary dissemination and the spread of lesions in the lung are not encountered where the case is properly selected and supervised. The patient with an exudative lesion, who may be acutely ill with definite pyrexia and toxemia should never be given heliotherapy but the one with a fibrotic lesion and positive sputum, or a case not improving on rest and hygienic treatment may be given sun baths to good advantage under adequate medical supervision. In my talks to medical students I list pulmonary tuberculosis as a contraindication to heliotherapy in order that they may err on the safe side if they err at all.

In these pulmonary cases we may expect (1) improvement in general condition, (2) decrease in lung moisture, "râles"; (3) decrease in sputum, it very often becoming negative, and (4) increased fibrosis.

Bone and joint tuberculosis presents probably the largest group of extra pulmonary cases which we are called upon to treat. The majority are accompanied by pulmonary lesions of varying degrees of severity. This factor alters the procedure of the heliotherapist only very slightly, as we have found that with proper treatment of the bone lesion, the pulmonary focus responds favorably as a rule.

Orthopedic measures must never be overlooked, and surgery plays a defi-

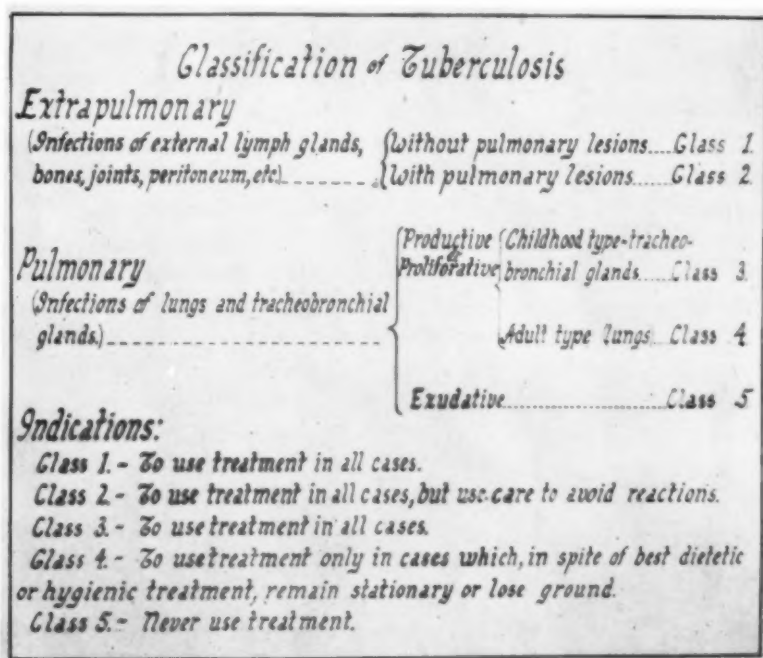


FIG. 2. Classification of tuberculous lesions from the heliotherapist's standpoint (Watson).

nite part in treatment. Before any surgical procedure is instituted, heliotherapy should be carried out for several months in order to bring the lesion to a quiescent state, if possible. Fusion and ankylosing operations and arthrodeses should then be followed by several more months of heliotherapy for the operation as such rarely removes the tuberculous focus but only gives added fixation to the joint involved. In the case of concomitant abscess and sinus formation these lesions repair quite readily under the influence of radiant therapy. Except in extremely early cases of joint tuberculosis, where erosion of the cartilage and destruction of bone has not as yet occurred, no attempt is made to secure a functioning joint. Where there has been bone destruction a firmly ankylosed joint gives much more insurance against future recurrence than a partly movable one.

Heliotherapy alone as an adjunct to rest and hygienic measures plus orthopedic sense gives good results, but only after an extremely long period of hospitalization. On the other hand, it is very necessary to return adults to industry as soon as possible, so the practice of aiding the above measures by a proper surgical procedure, and thus shortening disability, is becoming more and more the accepted policy.

Tuberculosis of superficial lymph nodes with and without softening and sinus formation responds well to heliotherapy. General body irradiation is the procedure of choice. It has been our practice to supplement heliotherapy with local X-ray to the glands involved. This hastens fibrosis and shortens the time required for cure.

Tuberculous pleuritis, with effusion, while an accompaniment of pulmonary tuberculosis, often clears with the aid of sun baths and I believe every case of pleural effusion (tuberculous) unless accompanied by a florid pulmonary lesion should have heliotherapy. This measure is reported as effective in preventing and remedying a tuberculous empyema.

Tuberculosis of the peritoneum is a secondary manifestation of a tuberculous lesion in the bowel, intra-abdominal or pelvic lymph nodes or pelvic organs. Rest and hygienic treatment plus heliotherapy over many months will produce a marked reduction in symptoms and local signs. Often it is possible, when the peritoneal lesion has become quiescent, to remove the primary focus, such as tube or appendix for instance, and then have the peritoneal process heal under a few more months of treatment.

Genito-urinary tuberculosis presents a complex picture unless the infection is unilateral or limited to a single organ which may be extirpated. When a unilateral renal tuberculosis is proven, the patient should have (1) heliotherapy during study, (2) the nephrectomy, and (3) further heliotherapy. Tuberculosis of both kidneys, or of the bladder or genitalia, demands prolonged rest and heliotherapy. Local lesions of epididymis may of course be removed, but the frequent complication of prostatitis, cystitis, or seminal vesiculitis calls for a long post operative course of treatment.

Tuberculosis of the skin in this country does not present the problem that it does in Europe. However, it is usually a local manifestation of a

systemic disease and, while not requiring as much rest therapy as do some other lesions, responds remarkably well to heliotherapy.

In treating local lesions of the middle ear, larynx and eye, as well as ulceration of the anus and lower rectum and lesions of the skin, the Kromayer lamp has proven of definite value as an adjunct to hygienic and rest treatment. In some European clinics these lesions are not treated locally at all but the patient is given general body radiation from the sun or carbon arc, with equally good results.

When one attempts to administer radiant energy as a therapeutic agent there are certain important factors which must not be overlooked. First of all, each patient is a new problem in therapeutics from the heliotherapist's standpoint. No two people react exactly the same to equal doses of light nor do two cases of tuberculosis present the same clinical features. Therefore, although an arbitrary plan of dosage may be adopted, the heliotherapist must individualize, and not attempt to carry through the same routine for every case. Secondly, too much irradiation, instead of being beneficial will be harmful by setting up reaction. The third factor to be observed is the reaction of temperature and pulse rate following irradiation. Immediately after an exposure to the sun, an elevation of body temperature is noted, which may reach one degree or more above normal. This must drop back to within one degree of normal within a half hour or the reaction is considered unfavorable and subsequent dosage must be reduced or insolation stopped entirely. We have

treated patients who could not take larger exposures than one minute at the start without reaction but who were able to gradually increase this and progressed satisfactorily. The pulse rate is likewise elevated after insolation. We require that within one half hour after exposure this rate must return to within twenty beats of its preinsolation rate. The body temperature and pulse reaction plus general condition of the patient, then, serve as our important "checks" on the progress of the treatment.

Rollier drew up an arbitrary norm which serves as the foundation for all heliotherapy prescriptions. (Figure 3.) His plan is to divide the body into five zones and expose each zone for a period of five minutes anteriorly and posteriorly until the patient is receiving a total of two to four hours insolation each day. The total varies with atmospheric conditions, the individual patient and the individual therapist. Some therapists advocate single daily exposures of two to four hours while others prefer shorter exposures, say forty-five to ninety minutes repeated after a period of rest. We feel that the exposures should be so regulated that tan production does not become intense. A ruddy erythema just bordering on a mahogany color is preferable to a tan which becomes almost chocolate brown, for this latter filters out a large part of the ultra-violet which we wish to have absorbed by the blood stream.

The question of the mercury arc versus the carbon arc is one which we believe can be definitely settled. It has been our experience that at the end of the sun season, patients are in much

better condition than they are in the following spring after several months of quartz mercury arc irradiation. On the other hand, a few patients who have had carbon arc irradiation have continued to progress during the winter months just as they did under solar irradiation. Since the mercury arc spectrum is rich in the short ultra-violet 2500 to 2700 \AA° and feeble in the range from 2800 to 3000 \AA° , and because the carbon arc using Sunshine Carbons gives a spectrum similar to that of the sun, 2800 to 8000 \AA° , we feel that the carbon arc is the artificial source to be preferred.

SUMMARY

1. Heliotherapy then is an important and necessary adjunct to the rest and hygienic treatment of tuberculosis.

2. It must not be overdone.

3. Patients must be insulated only under observation.

4. Graduated daily exposure individualized for each case must be the procedure of choice and safety.

5. Selected cases of pulmonary tuberculosis may safely be irradiated with benefit.

6. Extrapulmonary tuberculous lesions are definite indications for heliotherapy.

7. The part of the electro-magnetic spectrum from 2800 \AA° (near ultra-violet) to 8000 \AA° (visible red) is that part which we believe to be the most beneficial in treating tuberculosis and therefore the carbon arc lamp is preferable to the quartz mercury arc.

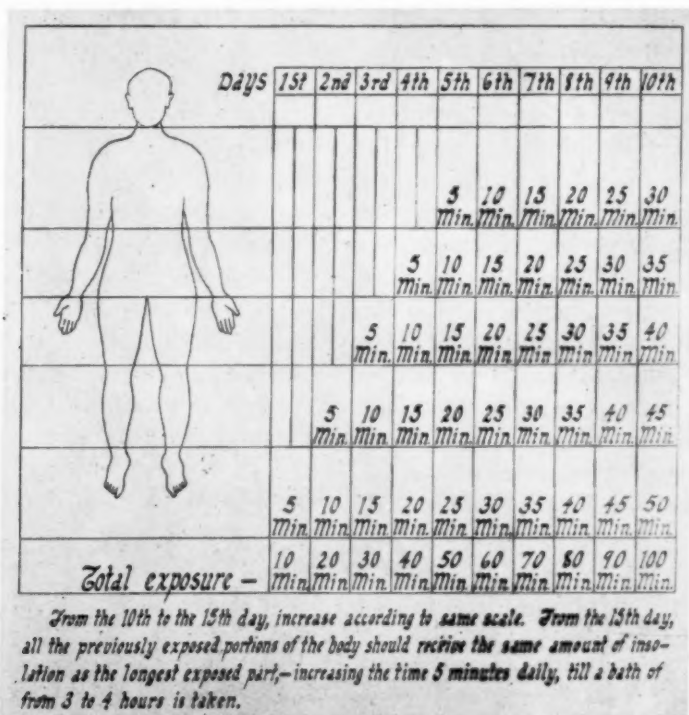


FIG. 3. Schedule of daily exposure for heliotherapy (Rollier).

BIBLIOGRAPHY

- ANDERSON, WM. T., JR.: Effective Ultra Violet, Arch. Physical Therapy, X-ray, Radium, II, Vol. IV, pp. 301-305.
- GOLDBERG, B.: Heliotherapy, City of Chicago Municipal Sanatorium Bulletin, Vol. X, Nos. 1, 2, 3, Jan., Feb., Mar., 1930.
- KIRKWOOD, R. C.: Value of Artificial Heliotherapy in Pulmonary Tuberculosis Arch. Physical Therapy, X-ray, Radium, Vol. VIII, No. 3, Mar., 1927.
- LAURENS, HENRY: Rôle of Light in Physiology & Pathology. New Orleans Medical & Surgical Journal, Vol. XXC, No. 6, pp. 380-389, Dec., 1927.
- Light in Tuberculosis. British Journal of Actinotherapy & Physiotherapy, Vol. IV, No. 7, Editorial p. 133, Oct., 1929.
- MAYER, EDGAR: Clinical Application of Sunlight & Artificial Radiation. 1926. Williams & Wilkins, Baltimore, Md.
- PHELPS, WINTHROP, M.: Specificity of Light Action in Tuberculosis. Journal of Bone and Joint Surgery, Vol. XII, No. 2, pp. 253-269. April, 1930.
- POLLOCK, WM. C.: Heliotherapy in Pulmonary Tuberculosis. American Review of Tuberculosis. Vol. 14, pp. 505-522. Nov., 1926.
- ROLLIER, A.: Heliotherapy. Frowde, Hodder & Stoughton, London, Eng.
- Heliotherapy of Surgical Tuberculosis Complicated by Pulmonary Tuberculosis. British Journal of Actinotherapy & Physiotherapy, Vol. IV, No. 7, pp. 140-143. Oct., 1929.
- WATSON, SAMUEL H.: The Use and Abuse of Heliotherapy in Tuberculosis. Journal A.M.A., Vol. 87, No. 13, pp. 1026-1031, Sept., 1926.
- WEINBREN, M.: Ultra-Violet Treatment in Chronic Pulmonary Tuberculosis. British Journal of Actinotherapy & Physiotherapy, Vol. IV, No. 7, pp. 137-140, Oct., 1929.
- WURTZEN, C. H.: The Treatment of Pulmonary Tuberculosis with Universal Light Baths. British Journal of Actinotherapy & Physiotherapy, Vol. IV, No. 7, pp. 135-137, Oct., 1929.

Mild Hyperthyroidism and the Neuroses*

By PHILIP S. SMITH, M.D., F.A.C.P., *Abingdon, Va.*

NO APOLOGY will be made for bringing to your attention a subject so frequently discussed in recent years as hyperthyroidism. Until the essential facts, both physiologic and pathologic, are more completely understood, the theme is not inappropriate for further study.

The caption of the paper suggests the limitations of the subject to be considered. That a well-defined and advanced hyperthyroidism presents no difficulty in diagnosis is indicated by the fact that pupil nurses frequently classify the patient upon admission to the hospital before the preliminary notes are made by the interns. In these patients thorough clinical investigation merely confirms the tentative diagnosis and affords an opportunity to estimate the degree of toxicity and the presence of visceral complications of the disease. Furthermore, an intensive study usually enables one to differentiate the two common types of hyperthyroidism—toxic adenoma and exophthalmic goiter, involving factors of importance in prognosis and possibly treatment.

Every well equipped hospital and,

*Read by invitation before the Alleghany-Bath Medical Society, Clifton Forge, Va., September 19th, 1930.

†From the Johnston Memorial Clinic, Abingdon, Virginia.

in this section of the State, practically every physician of average experience, is familiar with the acutely toxic patient. Equally, if not more numerous is that group with indefinite or incomplete evidence of thyroid overactivity presenting a much more difficult diagnostic problem.

It is my purpose to discuss briefly some phases of the similarity of mild hyperthyroidism and the conditions generally described as neuroses and psychoneuroses.

Of the intimate inter-relationship existing between the functions of many of the ductless glands there is ample proof. Unfortunately for the patient and the medical profession, this fact has been capitalized by many manufacturers and dispensers of so-called "pluriglandular" products with attractive, but unscientific, arguments supporting their therapeutic employment. But this does not invalidate the evidence of a common factor, such as sudden fright or great emotion, augmenting conjointly the activity, for example, of the thyroid and suprarenal glands during the period of stress. In such functional states the rôle played by the autonomic, or vegetative, nervous system is fairly well understood.

In the less sudden and acute conditions that provoke chronic fatigue, worry, anxiety, introspection, depres-

sion and hysteria there is also evidence oftentimes of a disturbed endocrine gland function influencing the sympathetic and vagal nerves; the converse also seems to be equally true. Just as the acute emotional states resemble in many respects traumatic or surgical shock, so the less pronounced psychoneurotic conditions have been termed "chronic shock."

For several years I have been interested in studying patients with exophthalmic goiter from the standpoint of a provoking factor of which the patient was conscious. We are familiar with the apparent sequence of a systemic infection and the inauguration of symptoms of Basedow's disease. In my experience where the exciting cause can be definitely elicited, it has been more frequently a sudden mental or nervous shock or "insult." An industrial disaster in a nearby town causing the death of many and vast property loss was offered by two patients as the explanation of the onset of their symptoms. Another woman dated her alleged "nervous breakdown" from a negro unexpectedly appearing at a nearby open window while she was using the telephone. These patients when examined some months later presented the classical picture of a high-grade exophthalmic goiter.

In 1926 I reported a review of a group of hypothyroid patients, of whom twelve young females had most of the symptoms and signs usually associated with a hyperthyroid state. All had lowered metabolic rates.

But I am considering now neither the acutely toxic patient nor the moderate hypothyroid, but rather those who give histories of nervousness, loss

of weight, goiter, tachycardia, palpitation, tremulousness, emotional instability and oftentimes diaphoresis, with slightly elevated metabolic rates.

Previous to the development of indirect calorimetry these individuals were oftentimes subjected to the "Goetsch test." If there was an unusual response to the subcutaneous injection of epinephrine, the thyroid gland was usually indicted as the cause of the patient's symptoms. Many such individuals, doubtless, were victims of a functional nervous condition associated with a pre-existing excessive function of the suprarenal glands. If so, their reaction to the injected agent can readily be explained.

Valuable as is the metabolism apparatus in differentiating the borderline hyperthyroid patient and the psychoneurotic, too much reliance can be placed in one series of tests. It is well known by those who have conducted many metabolic tests that neurotic individuals are prone at first to give moderately elevated rates. Their co-operation usually is poor and it is difficult for them to relax sufficiently to meet the requirements of a basal state.

With a view to enhancing the importance of the clinical investigation and evaluating the symptoms and signs of these patients, Dr. James H. Smith, of the McGuire Clinic, has formulated and employed the following table of relative values arbitrarily assigned:

Nervousness	1
Tremor (fine)	2
Loss of weight (5% or more)	3
Tachycardia (90 per min. or more)	4
Exophthalmos	5
Goiter	6
	—
	21

He believes that if the total result of the above values in a given patient exceeds 10 the diagnosis of hyperthyroidism is fairly well established and the metabolic rate will usually be found above plus 20. The above formula is of undoubted value, but in a country where adolescent thyroid enlargement and simple goiter are quite common, neurasthenic individuals are frequently seen who may have all of the above findings except exophthalmos. They often have a slightly elevated metabolic rate at the first observation, but subsequently are found to have no primary thyroid disease of an organic type. Many of these patients have been advised that their goiter is responsible for their symptoms, and the consequent fear of operation or long periods of disability brings them to the physician or surgeon for advice. Others have harbored for years morbid fears of other diseases.

Many neurotic patients are young women who have been married within recent years. The roseate glow of the post-marital stage has been replaced by the advent of children, worries and apprehensions. Confining and burdensome housework and oftentimes insufficient funds with which to balance the family budget result. Confronted with daily problems of this sort, with no solution to rectify them, a vicious circle is established. Such individuals, especially if they have a friend or relative who has a toxic goiter, may simulate unconsciously the hyperthyroid symptoms in a remarkably accurate manner. The premature suggestion of the family physician that possibly the goiter present since childhood or adolescence may be responsible

for their symptoms greatly adds to the difficulty. If a single metabolic test is done, the resulting rate, in the absence of a basal state, is apt to be slightly or moderately elevated. The administration of an iodine solution at this stage further confuses the clinical problem. A subtotal thyroidectomy will probably sentence the patient to a long term of invalidism with the same symptom-complex as previously.

During the past year I have been impressed with the increasing number of patients with such a syndrome coming to my attention. The recent industrial and financial depression may be a contributing explanation. Some of them were young married women who at the time of examination, or subsequently, were found to be harassed by marital unhappiness having a sexual basis.

No diagnostic "yardstick" is applicable to all such patients. Each one presents individual problems for solution. Disappointments naturally are encountered in apprehending the causative factors in some and their removal in others.

The investigation involves much patience, painstaking effort and sufficient time. Nothing, I believe, is more essential than a carefully recorded, detailed history of these individuals. The probability of successfully ferreting out the latent or occult contributory causes, of which the patient herself may not be conscious at the time, is increased if the family and friends are excluded. Otherwise the patient is apt to repress some confidential matter of importance. One such, a young married woman, who denied repeatedly in the presence of

her husband any marital or domestic difficulties, later wrote me of her restraint and reticence. When her husband's attentions to a neighboring feminine competitor of his wife ceased, the latter's thyroid symptoms and slightly elevated metabolic rate promptly disappeared.

The physical examination of these patients is of equal value in arriving at a correct estimate of the problem. Are the complaints of tremulousness, tachycardia, diaphoresis, etc., confirmed? Does the goiter present a bruit, thrill, and has it other characteristics of a toxic adenoma or hyperplastic thyroid? Is the systolic blood pressure increased—the patient's age and other factors generally associated with a systolic elevation considered? This point I wish to stress. The blood pressure observation should be repeated, if initially elevated, until it can be read with the patient relaxed; otherwise the increased pulse pressure may be influenced by psychic factors. The frequent association of an increased pulse pressure with hyperthyroidism is important and not generally considered. Its absence lends weight to a functional state. The chart will illustrate this point. The exceptions found in both groups will indicate that the cases were not selected, but chosen at random. The tables give more detailed information regarding the fifty patients composing each group. It will be noted that the average pulse pressure of the hyperthyroid is 25 mm. (or approximately 65 per cent) greater than that of the average neurotic patient. As expected, the average age of the toxic goiter patient is greater than the neurotic. The fre-

quent association of chronic foci of infection in both groups is interesting and of significance therapeutically.

After the foregoing statistics were compiled, the following statements by Dr. W. M. Boothby came to my attention:

1. "As pointed out by Plummer, adenomatous goiter with hyperthyroidism is not infrequently associated with hypertension as evidenced clinically by an elevated diastolic blood pressure ranging from 85 to 120 mm."

Only one of our fifteen cases of toxic adenoma charted had a diastolic pressure above 90 mm.

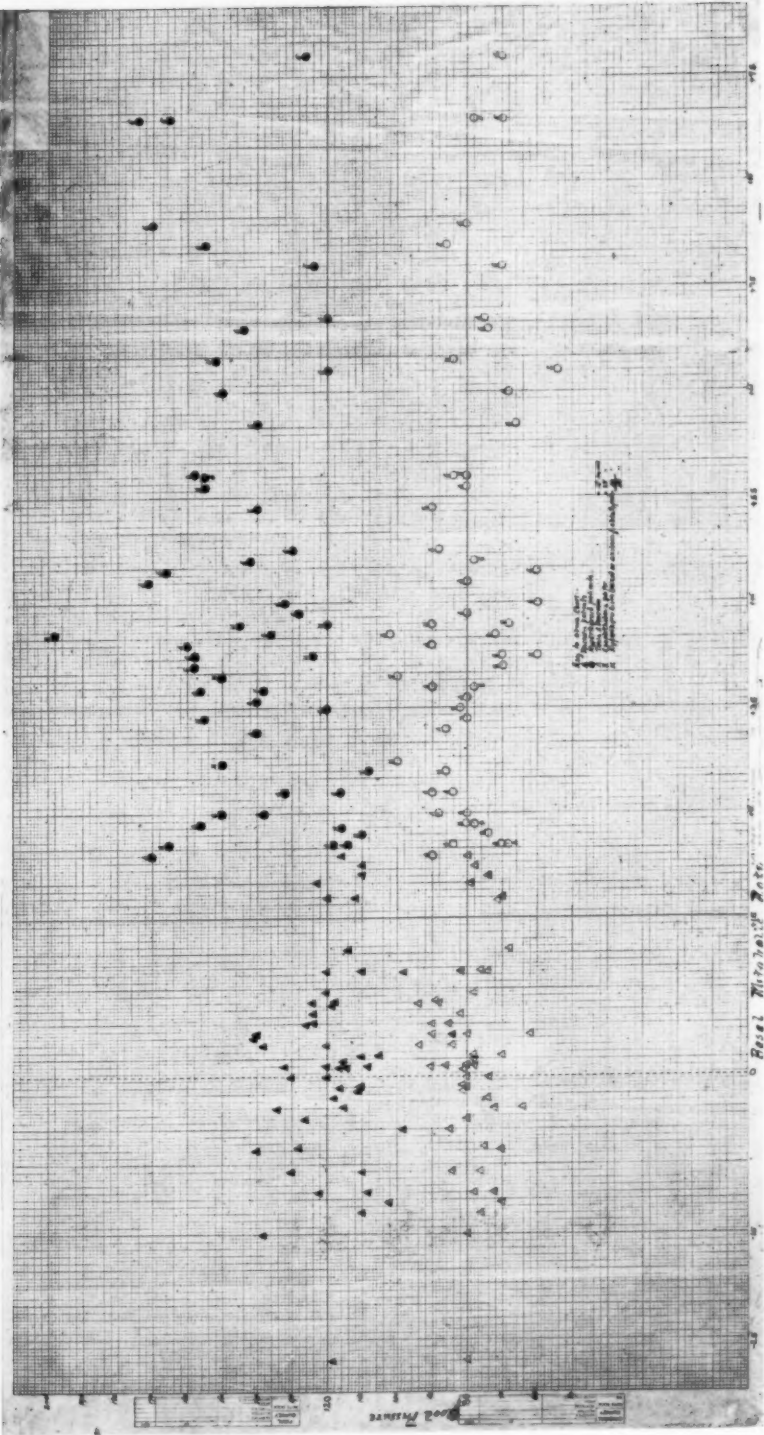
2. "In the absence of hypertension (diastolic), there will be an increase in the systolic and pulse pressures commensurate with the increase in metabolism."

With a few striking exceptions, this observation is confirmed in the cases of toxic adenoma shown.

Referring to patients with exophthalmic goiter, Dr. Boothby further states:

1. "If the diastolic pressure is low, the systolic pressure may be either normal or slightly increased. On the other hand, if the diastolic pressure is normal or increased, the systolic pressure will be distinctly elevated, as a high pulse pressure is necessary in order that the increased blood flow required by an elevated metabolism may be maintained."

Of the thirteen patients with exophthalmic goiter having diastolic pressures less than 80 mm., eight (61.6 per cent) show systolic pressures 140 mm. or above. Of the remaining twelve cases with diastolic pressures 80 mm.



Key to above chart:
● Neurotic Patients
▲ Hyperthyroid Patients
△ Toxic Adenoma
○ Euthyroid Goiter
□ Hyperthyroidism (mixed or unclassifiable types)

— 15 cases
— 25 cases
— 10 cases
— 50 cases

TABLE NO. 1—NEUROSES

CASE	SEX	AGE	SBP	DBP	PULSE METABOLIC		COMPLICATING DISEASES:—
					PRESSURE	RATE	
1.	F.	21	118	88	30	+ 7%	Chr. tonsillitis, myocarditis
2.	F.	55	140	90	50	+ 4%	(Chr. tonsillitis, visceroptosis, mucous colitis)
3.	F.	23	114	78	36	+ 1%	None
4.	F.	17	138	80	58	-15%	Hypothyroidism
5.	F.	20	116	80	36	+ 1%	Malnutrition
6.	F.	17	110	78	32	+20% (?)	(Goiter, arrested mental development, intestinal parasites)
7.	F.	24	120	74	46	0	Chr. tonsillitis
8.	F.	17	128	85	43	- 7%	(Chr. tonsillitis, appendicitis, Eye-strain, cardiospasm)
9.	F.	24	110	80	30	- 1%	Chr. tonsillitis, aerophagia
10.	F.	27	112	70	42	+17%	Hyperthyroidism (?)
11.	F.	35	98	85	13	- 5%	(Chr. tonsillitis, pyorrhoea, chr. pelvic infection)
12.	F.	21	124	85	39	+ 5%	(Goiter (simple), chr. tonsillitis, eye-strain.)
13.	F.	37	118	74	44	- 2%	Cr. tonsillitis, appendicitis
14.	M.	41	114	68	46	+12%	Chr. tonsillitis, myocarditis
15.	F.	36	120	82	38	+10%	Chr. tonsillitis, appendicitis
16.	F.	39	138	94	44	- 3%	Menopause
17.	F.	32	110	74	36	+19%	(Chr. tonsillitis, sinusitis, hyperthyroidism (slight))
18.	M.	22	108	78	30	+ 1%	Chr. tonsillitis, eyestrain
19.	M.	22	120	90	30	+ 1%	Chr. sinusitis, otitis media
20.	F.	40	116	80	36	+21%	Hyperthyroidism (mild)
21.	F.	30	116	80	36	- 1%	Goiter (simple), chr. tonsillitis
22.	F.	39	134	82	52	- 3%	None
23.	F.	40	118	80	38	-27%	Hypothyroidism, dental abscesses
24.	F.	56	110	76	34	-13%	Hypothyroidism, cholecystitis
25.	F.	26	110	76	34	- 9%	Pelvic infection
26.	M.	17	115	86	29	+ 1%	Goiter (simple), eye-strain
27.	F.	19	108	78	30	-11%	(Hypothyroidism (post-op.), obesity, chr. tonsillitis)
28.	F.	27	115	64	51	- 3%	None
29.	F.	19	105	70	35	+ 2%	(Goiter (simple), chr. tonsillitis, mitral stenosis)
30.	F.	24	98	74	24	+10%	Hypo-pituitarism, ovarism
31.	F.	26	130	80	50	0	Chr. tonsillitis, pregnancy
32.	M.	29	126	90	36	+ 5%	None
33.	M.	55	132	80	52	+ 1%	Achlorhydria, varicocele
34.	F.	37	102	70	32	-10%	Hypothyroidism, pulmonary t. b.
35.	F.	39	124	94	30	+ 7%	(Chr. tonsillitis, pyorrhoea, Chr. sinusitis)
36.	M.	22	110	76	34	+10%	Chr. tonsillitis, pyorrhoea
37.	F.	28	120	70	50	+17%	(Hyperthyroidism (mild), dental abscess)
38.	F.	26	110	80	30	- 1%	(Chr. tonsillitis, pyorrhoea, paroxysmal tachycardia)
39.	M.	33	123	89	34	+18%	Thyrotoxicosis (mild).
40.	M.	35	120	88	32	+ 8%	Pyorrhoea, chr. nephritis
41.	F.	36	120	84	36	+ 3%	Chr. tonsillitis, sinusitis, obesity
42.	F.	34	126	80	46	- 4%	Chr. endocervicitis
43.	F.	31	122	72	50	-11%	Subthyroidism, subovarium
44.	F.	45	140	70	70	- 7%	Subthyroidism, chr. hepatitis
45.	F.	28	110	78	32	+ 2%	Eye-strain
46.	M.	41	124	82	42	+ 6%	Chr. tonsillitis
47.	F.	43	130	84	46	- 9%	Chr. tonsillitis, menopause
48.	M.	51	84	62	22	+ 4%	Dental abscess, myocarditis
49.	M.	28	140	80	60	+ 4%	None
50.	F.	20	118	88	30	+ 7%	Chr. myocarditis, appendicitis

SUMMARY:—Females, 38

Males, 12

Average age 31.1 years

Average pulse pressure 38.7 mm.Hg.

TABLE NO. 2—HYPERTHYROIDISM

CASE	SEX	AGE	SBP	DBP	PULSE METABOLIC		COMPLICATING DISEASES:—
					PRESSURE	RATE	
						(all plus)	
1.	F.	53	140	80	60	36%	Chr. myocarditis, nephritis
2.	F.	25	132	90	42	27%	Chr. appendicitis
3.	F.	23	120	68	52	43%	Chr. appendicitis
4.	M.	34	138	88	50	25%	Chr. tonsillitis
5.	F.	53	118	68	50	22%	Chr. tonsillitis, cholecystitis
6.	F.	56	160	90	70	41%	Oral sepsis, chr. myocarditis
7.	F.	70	170	80	90	47%	Mitr. endocarditis, auric, fibril.
8.	F.	27	140	86	54	33%	Chr. tonsillitis, appendicitis
9.	F.	46	156	90	66	37%	Oral sepsis, sec. anemia.
10.	F.	32	155	80	75	56%	Chr. tonsillitis, perident. infection
11.	F.	58	198	102	96	42%	(Chr. tonsillitis, oral sepsis, art. hypertension, card. hypertrophy)
12.	F.	42	114	70	34	22%	Rheum. arthritis, chr. appendicitis
13.	F.	48	156	78	78	24%	(Chr. sinusitis, perident. infection, cholecystitis, appendicitis.)
14.	F.	39	120	75	45	72%	Chr. tonsillitis, alveolar abscess, (cholecystitis, appendicitis)
15.	F.	35	155	80	75	34%	Chr. tonsillitis
16.	F.	42	170	90	80	21%	Chr. tonsillitis, uterine, fibroid
17.	F.	44	150	68	82	65%	Chr. tonsillitis, perident. infection
18.	M.	33	140	66	74	62%	Iodine intolerance
19.	F.	27	128	80	48	44%	Perident. infection, appendicitis
20.	F.	41	130	88	42	50%	Chr. tonsillitis, appendicitis
21.	F.	23	116	84	32	27%	Chr. tonsillitis
22.	F.	61	164	84	80	22%	Oral sepsis, tonsillitis, cholecyst.
23.	F.	52	174	70	104	91%	Chr. myocarditis
24.	M.	22	158	70	88	39%	Chr. tonsillitis, rhinitis
25.	F.	19	142	78	64	49%	Chr. tonsil., sinusitis, appendicitis
26.	F.	17	132	60	72	45%	Chr. tonsillitis
27.	F.	21	155	86	69	79%	Dental caries
28.	F.	24	165	60	105	48%	Chr. tonsillitis
29.	F.	24	138	78	60	37%	Pelvic infect., perineal laceration
30.	M.	42	145	90	55	43%	Chr. tonsil, myocardi., oral sepsis
31.	M.	24	150	100	50	30%	Chr. tonsil., nephritis, bronchitis
32.	F.	36	115	80	35	24%	Chr. cystitis, pyelitis, oral sepsis
33.	M.	29	124	60	64	40%	Chr. appendicitis
34.	F.	22	110	74	36	23%	Pylorospasm
35.	F.	49	152	84	68	68%	Chr. cholecystitis, appendicitis
36.	M.	46	150	100	50	38%	
37.	F.	39	155	84	71	57%	(Chr. tonsil., perident. infection, chr. cholecystitis, appendicitis)
38.	F.	37	120	82	38	35%	Chr. tonsil, oral sepsis, mitr. stenosis
39.	M.	50	150	80	70	25%	Cardiac hypertrophy
40.	F.	52	126	70	56	97%	Chr. tonsillitis, peri-arthritis
41.	F.	28	155	80	75	57%	Chr. tonsillitis, pregnancy (early)
42.	F.	16	136	72	64	42%	None
43.	F.	42	165	88	77	91%	Chr. tonsillitis
44.	M.	22	158	70	88	40%	Chr. tonsillitis, rhinitis
45.	M.	24	144	74	70	71%	Chr. tonsillitis
46.	F.	56	140	90	50	54%	Chr. myocarditis, fibrillation
47.	M.	23	120	54	66	67%	None
48.	F.	33	124	70	54	77%	None
49.	F.	43	170	80	90	81%	None
50.	F.	24	108	86	22	29%	Peridental abscess

SUMMARY: Females, 39

Males 11

Average age 36.5 years

Average pulse pressure 63.7 mm. Hg.

or above, eight (66.6 per cent) have systolic pressures of 140 mm. or above.

2. "In the differential diagnosis between exophthalmic goiter and adenoma with hyperthyroidism the presence of hypertension (diastolic) is strong evidence that the hyperthyroidism is due to adenomatous goiter because hypertension (diastolic) is rarely found in patients with exophthalmic goiter."

Of the forty patients charted having either toxic adenoma or exophthalmic goiter, only six have diastolic pressures 90 mm. or above; of the six, five are of the adenomatous type.

3. "An increased pulse pressure in the absence of hypertension, and associated with an increased pulse rate, without many exceptions indicates an increased circulatory rate which, in turn, signifies an elevated basal metabolic rate. If hypertension is present, however, and especially if marked, a high pulse pressure and rapid heart are not necessarily indicative of an increased circulation rate and increased metabolism."

The pulse rates of our hyperthyroid patients are not shown in the tables, but most had tachycardia. The chart indicates that the general trend of the metabolic rates increases commensurately with the pulse pressures. The number of striking exceptions, however, would render questionable the statement that the metabolic rate, even in the absence of diastolic hypertension, can be predicted from the pulse rate and pulse pressure.

It is realized that the preceding analysis is somewhat irrelevant to the subject of this paper; that the number of patients in each group of hyperthyroidism is too small to justify

definite conclusions; and, finally, in any clinic the accuracy of a classification of hyperthyroid patients, especially those not operated, into the two major groups is open to question.

After the routine examination of the patient is made the patient should be kept under observation. The details of the metabolic test must be explained before it is begun, emphasizing their simplicity, the necessity of co-operation, and the influence of anxiety in contributing to an erroneous rate. Much can be learned by the conscientious and experienced technician while making the tests. Relaxation and co-operation in a psycho-neurotic are ordinarily more difficult to obtain than in a hyperthyroid. Usually, however, in the former the functional features of the patient's behavior become apparent during the test; they are prone to exaggerate the technical difficulties and record weird tracings. A metabolic test giving a rate initially elevated should be repeated each morning until the necessary co-operation is given in a manner satisfactory to the technician and clinician.

Psycho-neurotics when confined within a hospital, separated from their family, friends and daily associations, frequently relax remarkably within a few days. The insomnia, tachycardia and nervous symptoms may magically disappear. Focal infections should be eradicated. If then the point is driven home convincingly to the patient that the thyroid disease has been disproved conclusively, and the real functional nature of the symptoms explained, with helpful suggestions relative to removing the cause of the complaints, the transformation is at times strik-

ing and gratifying. Unfortunately, however, even after the diagnosis is reached, the domestic, financial or marital problems cannot be corrected invariably. In such cases improvement is problematical.

In conclusion, it is admitted that the comparatively simple procedures enumerated will not always remove the veil of uncertainty from the mind of the physician in every case presenting

the diagnostic problem discussed. But if this paper will serve to restrain the surgeon from premature subtotal thyroidectomy in the neurotic, and the medical man, or internist, from too quickly consigning a moderate hyperthyroid patient to the unenviable category of a hypochondriac, the effort will not have been fruitless. For of such (victims) is the kingdom of chiropractic and other cults.

REFERENCES

¹SMITH, PHILIP S.: Lowered Metabolic Rates, with Special Reference to Young Women. *Sou. Med. Jour.*, Oct., 1926.

²SMITH, JAS. H.: The Basal Metabolic Rate in Relation to Symptoms and Signs

in Hyperthyroidism. *Arch. Int. Med.*, Vol. 41; 96, June, 1928.

³BOOTHBY, WALTER M.: *Diagnosis and Treatment of Diseases of the Thyroid.* Oxford Med. Vol. 3.

Scurvy in the Presence of Thyrotoxicosis*

By R. H. KAMPMEIER, M.D., F.A.C.P., Pueblo, Colo.

A SEARCH of the literature available to me has failed to reveal a case report in which this peculiar association of diseases occurred.

The patient whose case is reported below showed a group of symptoms and signs which confused the diagnosis so that, though scurvy was considered at once, the thyrotoxicosis was not appreciated at first.

Case Report

Case Report—J. T., a Spaniard aged 52, barber by occupation, entered the Pueblo Clinic on April 5, 1930, and was referred to me by Dr. H. A. Black.

Chief Complaint—Diarrhea, fever, and weakness.

Present Illness—In December, 1929, the patient had had a routine physical examination and was apparently well. In January, 1930, he had a severe "cold", since which time he had had a persistent cough, which was non-productive.

From the onset of the illness in January there had been a persistent, gradual loss of weight. The appetite was good until about two weeks before admission, when it became very poor. The weight before the illness had been 119 pounds; the patient stated he had lost about 30 pounds in weight.

Some weeks after the onset of the illness a diarrhea developed, so that six or seven watery stools were passed daily. The stools contained mucus, but no blood, and only slight abdominal pain occurred at times. He

was greatly troubled with flatus. Because of the diarrhea, though the appetite was good, he limited his food to bread, toast, milk, tea, coffee, cereals, and at times eggs. He ate practically no fresh meat, except very occasionally, and fresh fruits and vegetables were used only at rare intervals and these, he said, passed through the bowel unchanged. Thirst had been marked from the onset.

Sweats appeared some weeks before admission to the clinic, and fever had been found by a physician who had seen him previously and, because of this and the cough, had considered pulmonary tuberculosis.

The patient had noted "spots" on the feet and legs on the day before admission.

Past History.—This was essentially negative.

Family History.—Wife and one child were alive and well.

Physical Examination.—The patient was a white male, of short stature and very emaciated. Weight was 90 pounds.

The head was negative. There was exophthalmos, which the patient said was present all his life. There was no lid lag, and no abnormality in wrinkling of forehead nor in convergence. Pupillary reflexes were normal. There was no apparent abnormality of the extra-ocular muscles. The conjunctivae were pale.

The tonsils were atrophic, and the pharynx appeared granular and red. The gums showed a marked degree of retraction and were spongy, with an advanced pyorrhea. In the neck the thyroid was palpable in both lobes, though there was no real enlargement.

There was a generalized lymphadenopathy. The nodes of the right posterior cervical

*From the Pueblo Clinic, Pueblo, Colo.

chain were 2-3 cm. in length and about 0.5 cm. in diameter. In the right anterior chain there were also several enlarged nodes. In both chains in the left neck were glands varying in size from a pea to one or more centimeters in diameter. Enlarged nodes were palpable in each axilla, up to the size of an almond. Both epitrochlear glands were about 1 cm. in diameter. The inguinal nodes were larger than average. All enlarged lymph nodes were freely movable; those in the right neck were quite firm and slightly tender.

The chest was of the asthenic type, somewhat emphysematous. Cardiac point of maximum impulse was 8 cm. from mid-line. The rate was 108 per minute; no murmurs were heard, but there were numerous extrasystoles. Expansion of the lungs was limited; the percussion note was hyperresonant; no abnormal breath sounds or râles were heard.

The liver edge was palpable. Genitalia were negative. There was some pitting edema over the ankles. The deep reflexes were normal. There was tremor of the fingers.

The skin was interesting for several reasons. The complexion was sallow. Over the wrists and dorsum of the hands was an orange colored discoloration, which had been present for years according to the patient. Over the dorsum of the feet and the lower half of the leg were copper colored areas about 0.5 cm. in diameter. Of greatest interest was a diffuse, fine petechial rash involving the dorsum of the foot, the whole leg and lower third of the thighs. The petechial spots were at the site of the hair follicles.

Technical Examinations. — Urinalysis showed specific gravity of 1.020, a trace of albumin and rare hyaline and granular casts. (Subsequently, after improvement, a concentration test showed nothing remarkable, the albumin and casts having disappeared.) Blood examination showed the following: hemoglobin 70%; red cells 4,300,000; white cells 12,800, with a differential of polymorphonuclears 89%, lymphocytes 9%, endothelial cells 2%. Arneith-Schilling count showed 20 young cells. Coagulation time

was two minutes (capillary tube) and platelets appeared normal on smear.

The blood Wassermann and Kahn tests were negative.

Roentgenologic examination of the chest demonstrated no disease of the lungs. Shadows appearing as if those of enlarged hilus glands were present.

Temperature upon first examination was 100.4 degrees.

Clinical Course.—The patient entered the hospital two days after the above data were collected. The symptoms had all persisted. The petechial rash had become more aggravated in intensity and distribution, and a scattering of petechiae had appeared upon the flexor surface of both arms in the elbow region. During the first four days in the hospital the temperature fluctuated daily from 99 to as high as 102 degrees. The diarrhea persisted the first three or four days.

A gland was removed from the right cervical region for biopsy. This was reported by the pathologist as showing merely a lymphadenitis.

Immediately upon hospitalization the patient was placed on a high vitamin diet, specifically receiving the juice of four to six oranges a day. The appetite improved at once, the diarrhea ceased and the temperature reached normal by the fourth day. No new petechiae appeared and those present faded rapidly in the first three days. The edema of the legs cleared.

The general improvement continued, though the pulse rate remained somewhat elevated and the complaint of weakness did not improve. About two weeks after improvement began a basal metabolic determination showed +47% which was checked two days later with the result of +36%.

Thyroidectomy was refused. After being absent from town for a time, the patient presented himself again three months after he was first seen. He had gained a total of 14 pounds. The pulse rate was still 120 per minute, there was tremor of the fingers. The size and character of the lymph nodes had not changed. The appetite had remained good and there had been no recurrence of diarrhea, fever, or petechial rash.

COMMENT

The numerous symptoms and signs which presented themselves upon the patient's admission made an immediate diagnosis impossible.

A provisional working diagnosis of lymphatic leukemia was made, trying to thus explain most of the presenting symptoms and signs under one disease picture. Thus asthenia, loss of weight, anorexia, fever, tachycardia, generalized lymphadenopathy and purpuric rash could be grouped to make up such a syndrome.

However, being struck by the petechial rash of the hair follicles as I had seen it in other cases of adult scurvy, I made a note to this effect, not accounting for the lymphadenopathy in this manner.

Leukemia was ruled out by the blood picture and biopsy revealed only a lymphadenitis, the serology was negative. The diarrhea, fever, anorexia and petechial rash responded at once to the administration of orange juice. It was only then that the thyrotoxicosis was recognized.

I believe this to have been an unquestionable case of scurvy in a patient with thyrotoxicosis. In some years of constant contact with large numbers of patients with thyrotoxicosis, I have never before seen scurvy as a complication. Not infrequently diarrhea accompanies thyroid toxicity, and this coupled with the inadequate diet of this patient undoubtedly accounts for the deficiency in vitamin C with the resultant occurrence of scurvy.

Editorial

STATUS THYMICO-LYMPHATICUS

Among the intrinsic pathological constitutions there is none possessed of more definite anatomical stigmata than those of *status thymicolymphaticus*. From medical antiquity the conception of lymphatism, or *status lymphaticus*, as a morphological-physiological type possessed of certain definite attributes, chiefly exudative, has been generally accepted. The frequent, almost constant, participation of the thymus in the morphological complex of this constitution has led to its more precise designation. The external bodily configuration found in *status thymico-lymphaticus* is far from constant. In childhood, those belonging to this constitution usually appear well nourished; the skin is soft and fine in texture, but pale, and a certain roundness of configuration, particularly of thorax and thighs is usually present. In more advanced years examples of this condition are found among well muscled brachymorphs with square frames, and very frequently, also, in asthenic dolichomorphs with slender long bones. In boys and young adult males there may be a certain femininity in bodily configuration and in distribution of body hair. When the bodies of those belonging to this constitution are examined at autopsy certain anatomical variations from the normal are found with great uniformity. The

thymus is hyperplastic or unduly persistent, or both hyperplastic and persistent. The hyperplasia involves both cortex and medulla, but especially the latter, and in the adult may be revealed chiefly by the large size of the thymic adipose tissue which has incompletely replaced the thymus although maintaining the form of the organ, throughout which small lymphoid islands with corpuscles of Hassall are distributed. Thus it comes about that a very frequent pathologic diagnosis in our records is that of fatty atrophy of a persistent hyperplastic thymus. There is also a general lymphoid hyperplasia which is noted particularly in respect to the tonsillar ring, the solitary and agminated lymphoid nodules of the gastro-intestinal tract, the mesenteric and retroperitoneal lymph nodes and the spleen. In the latter, particularly, the large germinal centers of the follicles may show a high degree of lymphoid exhaustion, particularly if some infection or intoxication has called for a marked production of lymphocytes. Equally constant are the changes in two other systems. The adrenals are hypoplastic, especially in respect to the chromaffinic tissue, and the cardio-vascular system is also hypoplastic. So surely do these changes occur in mutual association in the thymico-lymphatic constitution that the prosector in a demonstration autopsy can predict with assurance the pathol-

ogical state of heart, aorta and adrenals when he lifts the sternum and views the enlarged or persistent thymus. It is with considerable surprise, therefore, that we find that Young and Turnbull (An Analysis of the Data Collected by the Status Lymphaticus Committee, The Journal of Pathology and Bacteriology, 1931, xxxiv, (March), 213-258), in a study conducted along modern statistical lines, reach conclusions considerably at variance with those just expressed. For instance, they state that an abnormally large thymus *in itself* cannot be considered to be indicative of "status thymico-lymphaticus" when no obvious cause of death is found post-mortem. Likewise they found little, if any, association between the weight of the thymus and the amount of lymphoid tissue in the various parts of the body, and no definite evidence of any concomitant general hyperplasia of lymphoid structures in the cases with an abnormally large thymus. In their material there was no evidence of an association between arterial hypoplasia and an abnormally large thymus. However, they are in agreement with the generally accepted opinion that in exophthalmic goiter (Graves' constitution) the average gross weight of the thymus is distinctly above the normal. Since the investigation upon which these conclusions were based was conducted in a thorough and painstaking manner and the data analyzed by approved statistical methods it is of interest to discover why there should be such variance from the accumulated opinion of many presectors who have done thousands of autopsies but whose beliefs were founded on impressions

and not upon weighted mathematical data. The answer is not hard to find. The special objects of the investigation undertaken by this Committee were to establish by means of a large series of weights and measurements the standards of weight for age, and proportion to body weight, of the normal thymus at all ages, and to investigate closely the precise cause of death in persons dying suddenly from unexplained or trivial causes where the only apparent abnormality was the presence of a large thymus. In pursuance of these objects, record cards were prepared calling for appropriate information. It is significant as showing a lack of appreciation of the constitutional pathology involved that these cards did not call for information about either the adrenals or the aorta. Of these cards 680 were available for analysis and, from these, 464 cases of which 279 were under 16 years of age, were selected as constituting a *normal* group from which the mean weight and variability of the thymus at different ages was to be determined. The weights and measures were recorded by a number of observers and there is no certainty that in each instance other mediastinal structures and particularly the pericardium were equally well dissected from the thymus before weighing. This is an extremely important point in respect to an organ as small as the thymus. To this "normal" group there were admitted cases, among others, in which death was due to trauma from accidents, firearms or burns, to hemorrhage at surgical operations; to poisoning by gas or inorganic or organic chemicals; to asphyxia during or after delivery, in infantile con-

vulsions or epileptic fits; and to anesthetics or operative shock. Many of these are precisely the conditions in which the thymico-lymphatic constitution might turn the scale to a fatal issue. Among the presumably "normal" cases, in the age group 1 to 6 years there appeared three thymuses of such unusual size (99.2, 84 and 70 grams) that the authors omitted them in computing the mean values for the group. This alone shows the intrinsic weakness of the fundamental data. It is not surprising, then, that values greater than those of other similar investigations and distinctly higher than those usually considered normal were obtained. The high values for standard deviations in each sub-group show how heterogeneous the supposed normal group was. For instance in the full-term foetuses the mean weight of the thymus was 21.83 ± 1.55 grams and the standard deviation, 12.78 ± 1.09 ; in age group 1-6 years, mean weight, 23.30 ± 0.86 grams, with standard deviation, 10.36 ± 0.61 ; 11-16 years, mean weight 33.91 ± 1.33 grams; standard deviation, 14.62 ± 0.94 . These means are from one and one-half to three times greater than those considered normal in the autopsy material under the supervision of the writer. It is our belief that any thymus exceeding 20 grams in weight is of pathological significance. Young and Turnbull recognized the difficulty with their normal material for they found that in ten instances the gross weight of the thymus exceeded the mean weight in the corresponding age-group by at least twice the standard deviation or variability. Since such a deviation is likely to occur fortuit-

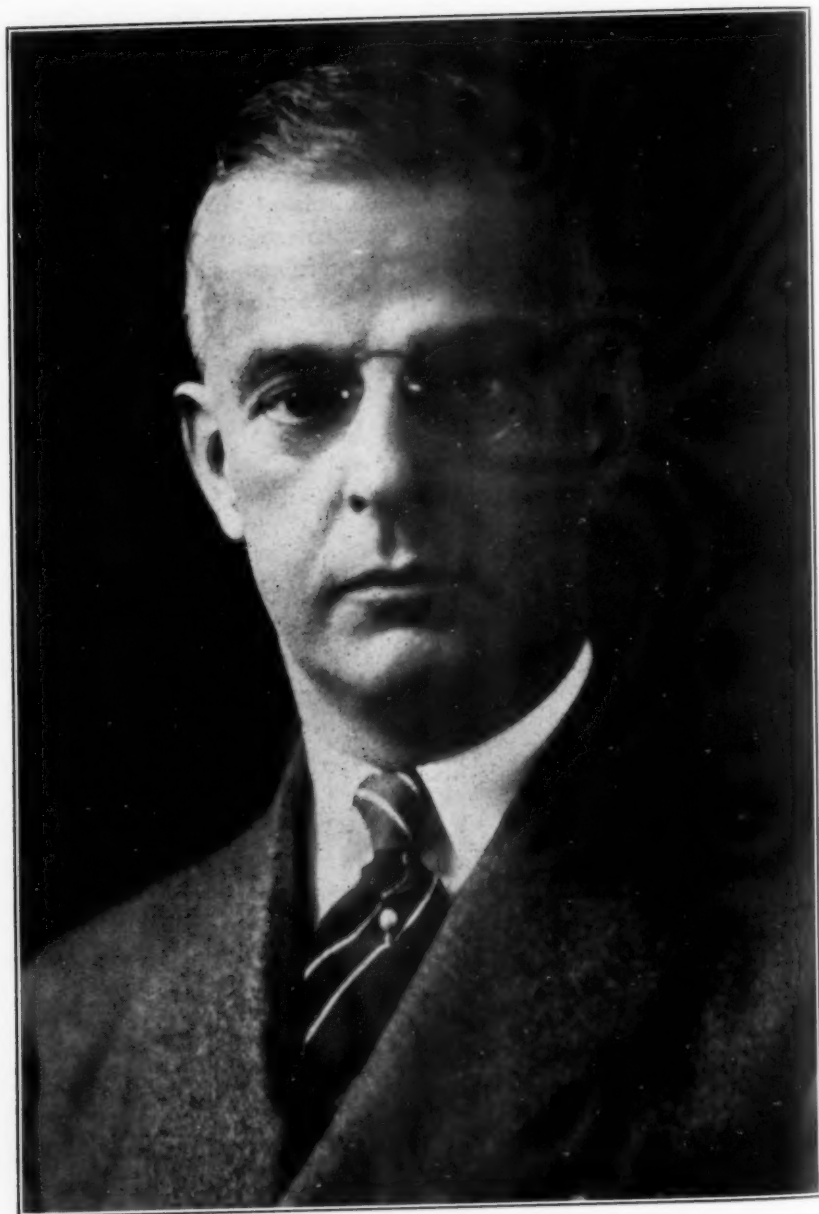
ously in approximately but 1 in 50 trials, they felt that all of these thymuses might properly be deemed to be abnormal in size. We can have but the greatest admiration for the extended mathematical analysis of the data collected by this Committee and full appreciation of the labor involved in their analysis, but it must always be borne in mind that the conclusions derived from a statistical study are no stronger than the original unit data upon which they are based. Much more rigid criteria must be set up and the full implication of the thymico-lymphatic constitution considered in selecting a group to serve as "normals" for the basic material of such an investigation.

THE TERCENTENARY OF CINCHONA

It is now about three hundred years since Cinchona bark was first made use of by Europeans. There is much evidence to show that the Indians of Peru were aware of its curative value before the arrival of the Jesuit missionaries, but the usual statement in regard to the first utilization of the bark by Europeans is the one which led to the application of the name *Cinchona* by Linnaeus. Having been appointed Viceroy of Peru in 1628, the Count of Chinchon went with his Countess to that country to take up his official duties. There they both suffered from fever and, in 1638, Don Juan de Vega, physician to the Viceroy, cured the Countess by administration of the bark at Lima. This event is depicted in three frescos in the Hospital de Santo Spirito in Rome, and through it and the early transportation of the bark to

Europe by the Jesuit fathers, the remedy was known for many years as Countess's Powder, Jesuit's Powder, and Cardinal's Powder. Henry S. Wellcome states decisively, however, in his foreword to the Souvenir of the Cinchona Tercentenary Celebration and Exhibition held at the Wellcome Historical Medical Museum during the past few months, that the tercentennial year should be 1930 and not 1938. He dates the first utilization of Cin-

chona in the treatment of an European to the former year, when Don Juan Lopez de Canizares, the Spanish corregidor of Loxa, was cured of intermittent fever by an Indian cacique who taught him the curative attributes of the bark and the method of administering it. Thus, although quinine was not isolated until 1820, Cinchona has now entered upon its fourth century of usefulness since it was first made known to our civilization.



SYDNEY R. MILLER, B.S., M.D., Baltimore, Maryland.
Retiring President

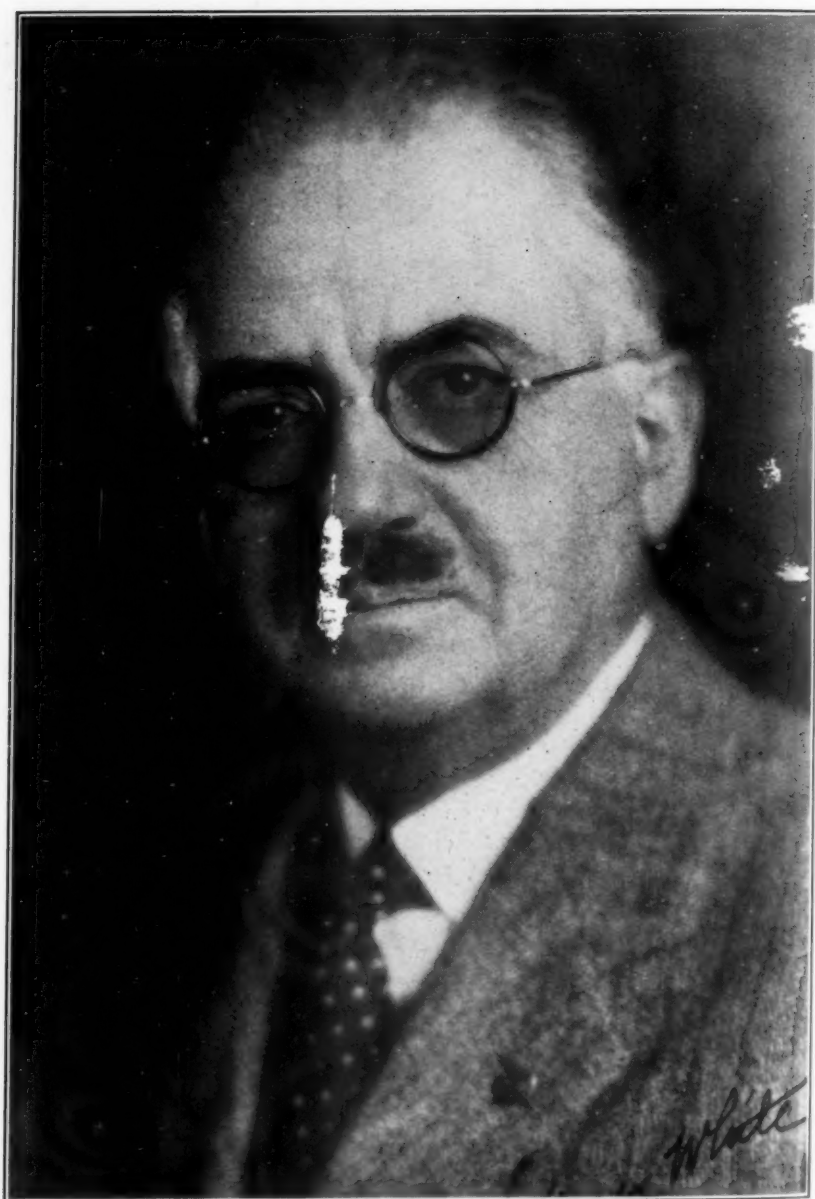
SYDNEY R. MILLER, B.S., M.D., Baltimore, Maryland.

Retiring President

AMERICAN COLLEGE OF PHYSICIANS

Born, 1884; B.S., New York University; M.D., Johns Hopkins University School of Medicine, 1910; Director of Laboratories, Phipps Psychiatric Clinic, 1912-14; Associate Clinical Medicine, Johns Hopkins University School of Medicine, 1910 to date; Assistant Professor of Medicine, University of Maryland School of Medicine; 1922 to date; Assistant Attending Physician, Johns Hopkins Hospital; Attending Physician and Member of Executive Committee, Union Memorial Hospital; Member, Zeta Psi, Alpha Omega Alpha, Phi Beta Kappa Fraternities; Member of the Baltimore Medical Society, Maryland State Medical Society, American Medical Association, Southern Medical Association, American Climatological and Clinical Association, Interurban Clinical Club, and a Fellow of the American College of Physicians since 1920. He is a life member of the College.

His Presidency of the American College of Physicians was marked by enthusiasm, foresight, energy and untiring effort in behalf of the College. Due chiefly to him the Baltimore Clinical Week was one of the most successful the College has ever held.



S. MARX WHITE, B.S., M.D., Minneapolis, Minnesota.
Newly Inducted President, 1931-32

S. MARX WHITE, B.S., M.D., Minneapolis, Minnesota.

Newly Inducted President, 1931-32

AMERICAN COLLEGE OF PHYSICIANS

Born, 1873; B.S., University of Illinois; M.D., Northwestern University Medical School, 1897; Post-graduate work at the University of Vienna and the University College Hospital of London; Demonstrator, Pathology and Bacteriology, University of Minnesota Medical School, 1898-00; Assistant Professor of Medicine at same institution, 1900-08; Associate Professor of Medicine at same institution, 1908-19; Professor of Medicine at same institution, 1900 to date; Member of Staff, Northwestern Hospital, 1908 to date, St. Mary's Hospital, 1919 to date, Abbott Hospital, 1921 to date; Eitel Hospital, 1926 to date; Member and ex-President of the Minnesota State Board of Health; Member, Nu Sigma Nu, Alpha Omega Alpha and Sigma Xi Fraternities; Member of the Hennepin County Medical Society, Minnesota State Medical Association, American Medical Association, Minnesota Academy of Medicine, Minnesota Pathological Society, Interurban Clinical Club, Association of American Physicians and a Fellow of the American College of Physicians since 1922.

Dr. White has been an active Fellow of the College from the beginning of his membership. He has been a member of the Board of Regents and a member of the Committee on Credentials for several years, a Vice President and the General Chairman of its Fourteenth Annual Clinical Session. Under Dr. White's able generalship the Minneapolis meeting in 1930 stands out as one of the most successful of the College.



FRANCIS MARION POTTENGER, Ph.B., Ph.M., A.M., M.D., LL.D.,
Monrovia, California.
President-Elect, 1931-32

FRANCIS MARION POTTENGER, Ph.B., Ph.M., A.M., M.D., LL.D.,
Monrovia, California.

President-Elect, 1931-32

AMERICAN COLLEGE OF PHYSICIANS

Born, 1869; Ph.B., Ph.M., A.M., LL.D., Otterbein College, Westerville, Ohio; M.D., Cincinnati College of Medicine and Surgery, 1894. Postgraduate study at New York Polyclinic and European Clinics, including Vienna, Berlin and London. Lecturer on Diseases of the Chest and Climatology, University of Southern California College of Medicine, 1903-04; Professor of Clinical Medicine, same, 1905-09; Professor of Diseases of the Chest, College of Physicians and Surgeons of the University of Southern California, 1914-20; President and Medical Director, The Pottenger Sanatorium; Member, Board of Trustees, Otterbein College; Member, Phi Rho Sigma and Pi Gamma Mu Fraternities; Member and ex-President, Los Angeles County Medical Association, Member and ex-President, Los Angeles Clinical and Pathological Society, Member and ex-President, Southern California Medical Society, Member, California Medical Association, Member, Pacific Interurban Clinical Club, Member, California Academy of Medicine, Member, Trudeau Society of Los Angeles, Fellow, American Medical Association, Member and ex-President, the American Therapeutic Society, Secretary, Association for the Study of Internal Secretions, Member, American Climatological and Clinical Association, Member, American Association for the Study of Allergy, Member, American Public Health Association, Member and ex-President, American Sanatorium Association, Member, American Heart Association, Member, Director and Vice President, Los Angeles Tuberculosis Association, Member National and International Association for the Study and Prevention of Tuberculosis, Member, Eugenics Society of the United States of America, Member, Association for the Advancement of Science, Member, Science League of America, Member, National Geographic Society, Member and Regent, Pacific Geographic Society, Member, American Academy of Political and Social Science, and a Fellow of the American College of Physicians since 1916. He is a Life Member of the College.

Dr. Pottenger has been a most productive writer, being the author of at least eight volumes dealing with various phases of tuberculosis. Several of his books have been published in from two to four editions. Of especial importance is his work on the vegetative nervous system and symptoms of visceral disease, now in the second edition.

Dr. Pottenger became a Fellow of the American College of Physicians almost at the beginning of its organization. Few members have as intimate a knowledge of the development of the College as he. He has been a member of the Board of Regents since 1923, and Vice President, 1929-30. Though far removed from the place of meetings of the College and its Board of Regents, he has been most regular in attendance through all these years, and has always held the welfare of the College foremost in his endeavors.

Abstracts

The Behavior of Lead in the Animal Organism, II. Tetraethyl Lead. By ROBERT A. KEHOE and FREDERICK THAMANN. (The American Journal of Hygiene, March, 1931, p. 478.)

Because of its peculiar physical properties which promote a different type of initial distribution in the tissues when it is absorbed as compared to the water-soluble compounds of lead, tetraethyl lead offers an especially interesting field for investigation. Its high selective affinity for fat-containing tissues and for the nervous system has been known for some time. Its wide distribution in a low concentration in motor fuels has raised the question whether there is absorption of lead through the skin of persons who come in contact with such gasoline, and whether lead thus absorbed may be expected to accumulate in nervous and other lipoid-containing tissues. Using rabbits in carefully controlled experiments, the authors found that tetraethyl lead is absorbed through the intact skin, but that this absorption is inappreciable when in solution in gasoline in amounts not in excess of 0.1 per cent. The initial distribution of the lead in the tissues in rapid tetraethyl lead absorption corresponds to that of an oil-soluble material and indicates that some portion of the tetraethyl lead is absorbed and circulates as such. However, tetraethyl lead is rapidly decomposed by the tissues so that, after a period of from three to fourteen days, all of the lead is distributed in a manner characteristic of water-soluble lead compounds, and excretion follows quantitatively that of water-soluble lead compounds. From this evidence, it is concluded that tetraethyl lead poisoning is not different from lead poisoning occasioned by other compounds of lead.

Miliary Lung Disease Due to Unknown Cause. By R. R. SAYERS and F. V.

MERIWETHER. (Public Health Reports, Vol. 45, No. 49, December 5, 1930, p. 2094.)

Of 18,285 individuals examined in connection with a systematic investigation for the study and control of silicosis and tuberculosis among miners, about 125 instances were found in which the roentgenograms appeared to be those of miliary tuberculosis, but the patients were, with two exceptions, apparently healthy. The cases ranged in age from 16 to 69 years. With one exception, an Indian, the subjects were all white, native-born Americans, most of whom came from rural districts or had worked in the harvest fields. Eight per cent had never worked in or around mines. Many of the subjects (65.6 per cent) gave no symptoms. Certain of the remainder had had cough, dyspnea, expectoration, hemoptysis (blood-tinged mucus), loss of strength, loss of appetite, night sweats, fatigue or pain in the chest. Upon X-ray examination, a decided enlargement of the hilum shadows was found in 91.2 per cent of the group. The most characteristic finding was the large number of discrete, dense, shotlike spots scattered over the lungs, in numbers ranging from less than 25 to more than 500 in each patient. In 94 per cent of the cases more than half of the spots were located in the bases, while in the other 6 per cent they were scattered about equally over the lung area. Two cases only showed tubercle bacilli in the sputum and 7 had four plus Wassermann tests. Unstained smears of 31 cases (all those examined) were positive for higher fungi, two types of which were identified, *Aspergillus fumigatus fisheri* and *Aspergillus niger*. Ten cases tested with antigen of the former gave negative reactions; of 6 cases tested with *Aspergillus niger* all gave positive results. Miliary tuberculosis, pneumoconiosis and calcium metastasis must be considered in differential diagnosis, to-

gether with pneumomycosis. The "miliary calcification of the lungs" reported by Sutherland is probably the same condition as that described here. These miliary calcifications may be due primarily to fungus infection.

Acute Mercury Poisoning: Report of Twenty-one Cases with Suggestions for Treatment. By B. I. JOHNSTONE. (The Canadian Medical Association Journal, April, 1931, p. 500.)

The main details in respect to 21 patients treated in the Henry Ford Hospital, Detroit, for acute mercury poisoning are outlined in this article. In 18 of the 21 cases, the bichloride was the compound responsible. The average age of the group was 30.8 years, and there were twice as many women as men. In four, poisoning was definitely accidental; six admitted having taken the drug with suicidal intent, and in the remainder definite information was not obtainable. In two cases, both fatal, poisoning was due to the use of bichloride solution as a vaginal douche. Vomiting occurred in 17 of the 21 cases. It began in from two minutes to one-half hour after ingestion and became frequent and distressing if large amounts of mercury had been taken. The vomitus was often blood stained. All patients showing evidence of toxicity had diarrhoea, beginning within a few hours, with liquid, bulky, extremely fetid, and later bloody, stools. There was marked tenesmus and the whole abdomen became tender, especially so along the course of the colon. By the third day salivation, stomatitis, glossitis, and gingivitis occurred. Oliguria was present in 6 patients and anuria in 2. When considerable absorption of mercury had taken place there was a rapid rise in the non-protein nitrogen of the blood, definitely established by the third day and reaching its maximum by the fourteenth day if the patient still survived. The highest figures were obtained in a patient who died 12 days after a single bichloride vaginal douche: non-protein nitrogen, 293 mg.; urea-nitrogen, 240 mg.; uric acid, 18.3 mg. per cent. In treatment, efforts should be directed chiefly towards prevention of absorption, for once the drug has reached the circu-

lation there is no effective antidote in spite of the long list of remedies proposed. In addition to the usual methods it is suggested that after gastric lavage a duodenal tube be passed and transduodenal irrigation carried out with warm saturated solution of sodium bicarbonate. By this method the whole intestine is washed out, removing that portion of the drug which has left the stomach. Gastric lavage and transduodenal irrigation at least once daily for several days thereafter will prevent reabsorption of at least a part of the mercury excreted. Using an ounce of a saturated solution of magnesium sulphate as a stimulant, biliary drainage was done for several hours on a number of patients in the hope of still further reducing reabsorption following excretion from the liver.

Changes in the Blood Sugar and Blood Phosphorus in Rabbits Following the Injection of Suspensions of Bact. Aertrycke. By M. E. DELAFIELD (The Journal of Pathology and Bacteriology, March, 1931, p. 177.)

As there is already experimental and clinical evidence that significant changes in the blood sugar occur in various infections it was thought to be worth while to discover whether changes in blood phosphorus are associated with the bacterial hyperglycemias and hypoglycemias. Suspensions of *Bact. aertrycke* and bacterial filtrates were injected intravenously into rabbits and blood sugar and phosphorus determinations made at frequent intervals. It was found that a hyperglycemia was first produced and that this was followed by hypoglycemia. When death occurred, it was in the hypoglycemic phase. Inorganic blood phosphorus was lessened in amount during hyperglycemia and increased again, often above the initial value, during the hypoglycemic phase. Organic acid-soluble blood phosphorus, on the other hand, in many cases increased during hyperglycemia and decreased during hypoglycemia. These changes in the sugar and phosphorus values are specific in the sense that they are entirely different from the results obtained by the intravenous injection of diphtheria toxin.

Reviews

Recent Advances in Biochemistry. By

JOHN PRYDE, B.Sc. (St. And.), M.Sc. (Wales), Lecturer in Physiological Chemistry, Welsh National School of Medicine, University of Wales. Third edition, with 42 illustrations. F. Blakiston's Son and Co., Philadelphia, 1931. Price, \$3.50 net.

In this edition there has been an extensive revision of the original subject matter and two new chapters have been added, one on "Protein Structure and Proteolytic Enzymes" and the other on the "Cholane Series," which includes the bile acids and sterols. On the other hand the chapters on "Colloids and the Physical Chemistry of Proteins" and on "Chemotherapy" have been omitted. The last-mentioned topic is now considered in another volume in the Recent Advances series, "Recent Advances in Chemotherapy" by Dr. W. G. M. Findlay. The volume under review covers a diverse selection of the more important recent advances in biochemistry, in particular those which serve to indicate the trend of present day research in this field. The main topics presented, in addition to the two previously mentioned, are Amino Acids and Urea Formation; Sulphur Compounds and Protein Metabolism; The Role of Tyrosinase; The Nucleo-Proteins; The Carbohydrates; The Biochemistry of the Fats; The Biochemistry of Phosphorus Compounds; The Vitamins; Haemoglobin and Related Natural Pigments; The Chemical Basis of Specific Immunological Reactions. Each chapter is followed by selected references to the sources of the new material presented. The style of this book is excellent and the free use of structural formulas and of diagrams makes for clear exposition. It can be recommended particularly to students who wish to supplement the material of the older textbooks and to those working in related fields such as Internal Medicine, Physiology and Pathology, who need to keep themselves informed upon the newer viewpoints in Biochemistry.

Calcium Metabolism and Calcium Therapy.

By ABRAHAM CANTAROW, M.D., Assistant Demonstrator of Medicine in the Jefferson Medical College, Philadelphia, 215 pages. Lea and Febiger, Philadelphia, 1931. Price \$2.50 net.

This monograph presents in a logical manner the present state of knowledge in respect to calcium metabolism. Although there is much that is still the subject of controversy in this field, the author has succeeded in giving a clear exposition of his subject matter, considering first the normal metabolism of calcium; then calcium metabolism as altered by disease; and finally, the therapeutic uses of calcium. Under each of these main divisions there are appropriate subdivisions covering the entire field of laboratory and clinical research germane to the subject. Such a treatise will doubtless require frequent revision, but its importance cannot be overestimated for, as the author states in the preface, "calcium metabolism occupies a position in current medical literature and thought comparable to that held by carbohydrate metabolism some years ago." While it is to be expected that parathyroid hormone, ultra-violet irradiation and vitamin D would receive full discussion, the inclusion of the less discussed therapeutic uses of calcium, such as in lead poisoning, is evidence of the completeness of the treatment of the subject. This book will be very useful to the practitioner who desires scientific guidance as to when and how calcium should, or should not, be used in the treatment of disease.

Epidemiological Essays. B. F. G. CROOKSHANK, M.D., F.R.C.P. The MacMillan Company, New York, 1931. Pages x + 136. Price \$2.50.

As the author shrewdly predicts in his prefatory note, the reviewer finds in this volume a collection of papers, all of which have appeared previously. Some of them had their first appearance more than ten

years ago and much that is of value has been added to the subjects discussed during those years. This is especially true of Acrodynia, which is brought up only to 1920, of Botulism and of Encephalitis Lethargica. Thus it is that if the reader judges these essays by their scientific content he is sure to be disappointed. Their value lies rather in the emphasis put upon the Hippocratic Epidemiology, in contrast to the modern statistical method of treating this subject; in interesting contributions to the History of Medicine, and in certain common-sense observations upon the foibles of therapeutic faddists who overlook the fundamentals of medical practice.

Intestinal Toxemia Biologically Considered.

By ANTHONY BASSLER, M.D., F.A.C.P.
With 16 text illustrations. F. A. Davis Company, Philadelphia, 1930. Pages xvi + 433. Price \$6.00 net.

This book develops more completely the author's theory and practice in regard to the biological aspects of intestinal toxemia, and is a fuller statement of the technical procedures involved, than was possible in his earlier texts. It represents, also, a fuller experience, covering therapeutic results in 5000 cases. The author pays his respects in no uncertain terms to the procession of fads which have been vaunted as cures for intestinal toxemia, such as colonic irrigations, Bulgarian bacilli, *Bacillus acidophilus*, purgations, mineral oil and now the ingestion of yeast. In place of these he advocates identification of the intestinal flora and the rectal or sub-cutaneous injection of vaccines and ectoantigens, of which he lists no less than 109 and 76 respectively. Much of the book deals, therefore, with bacteriological methods and four large folding tables are employed to present this data. The conclusions are those of an enthusiast and for the greater part are presented without supporting evidence. Few readers will be willing to accept as facts such assertions as that the in-

testine is the source of the original infection in the vast majority of all cases of both acute and chronic endocarditis; that practically every case of chronic myocarditis is a neglected case of intestinal toxemia, or that more chronically infected tonsils occur from the intestine than from the pharyngeal surface. It is unfortunate that such a well-printed book should have illustrations that are as inferior as the group reproducing photomicrographs of intestinal pathology. These might easily be improved and many loosely written sentences should be recast if a second edition appears.

Potter's Therapeutics, Materia Medica and Pharmacy. The Special Therapeutics of

Diseases and Symptoms, the Physiological and Therapeutical Actions of Drugs, the Modern Materia Medica, Official and Practical Pharmacy, Prescription Writing, and Antidotal and Antagonistic Treatment of Poisoning. By SAM'L O. L. POTTER, A.M., M.D., M.R.C.P. Lond.; Fifteenth Edition, revised by R. J. E. SCOTT, M.A., B.C.L., M.D., xv + 997 pages. P. Blakiston's Son & Co., Philadelphia, 1931. Price in cloth, \$8.50.

The fifteenth edition of this well-known reference book follows the general plan of those which preceded it. Much new material has been added and certain sections which had become obsolete have been deleted. It is intended to be a compendium of concise information regarding both official and non-official drugs and preparations; and this expectation is met in a most satisfactory manner. For busy physicians, particularly those who through choice or necessity do their own dispensing, and for pharmacists, this work will continue to be of great value. The alphabetical arrangement, thumb index to major divisions, conveniently placed tables and an unusually complete index increase its usefulness and make its subject matter readily available.

College News Notes

THE AMERICAN COLLEGE OF PHYSICIANS

FINANCIAL STATEMENTS

FOR 1930

Summarizing the Financial Reports, it may be stated that gross income for the year ending December 31, 1930, amounted to \$74,834.59 (1929—\$68,946.83), and that the net expenditures amounted to \$51,619.80 (1929—\$47,584.44), leaving a balance of \$23,214.79 (1929—\$21,362.39); \$3,100 (1929—\$1,200) of which is added to the Endowment Fund and \$20,114.79 (1929—\$20,162.39) added to the Principal of the General Fund. During the year, the Endowment Fund, made up of Life Membership subscriptions, was increased from \$5,300 to \$8,400; and the General Fund increased from \$60,624.07 to \$80,738.86, making the total assets of the College as of December 31, 1930, \$88,338.86 (1929—\$65,924.07).

The cost of conducting the Minneapolis Clinical Session was \$11,320.23, which was reduced through profits on the Commercial Exhibits and guest fees by \$7,946.90, or a net of \$3,373.33 (Boston, 1929—\$3,664.93).

The Annals of Internal Medicine for the calendar year showed a gross cost of \$19,754.65 and a gross income of \$19,155.00, or a net deficit of \$599.65. This deficit would be eliminated if a reasonable valuation were placed on the surplus stock. The net advertising profit on the Journal was \$3,543.49, as compared with \$2,263.46 for 1929. Actually Volume III, completed with the June, 1930, issue, showed a surplus of \$561.19, the first time in the history of the Journal that a credit balance had ever been shown—and this, too, after the Journal has been constantly improved and enlarged.

It should be pointed out that the amount of traveling expenses not only on the account of the Annual Clinical Session, but also on the account of the Executive Secretary's Office, includes the traveling expenses of the Officers and Regents to the meetings officially called for the Board of Regents.

In addition to \$43,036.70 (1929—\$26,820.60) invested in securities (see Schedule No. I), \$22,523.20 is carried in Savings Accounts and \$20,654.00 is in Checking Accounts (per complete statements filed by the Auditor).

Clement R. Jones, Treasurer
E. R. Loveland, Executive Secretary

College News Notes

1487

AMERICAN COLLEGE OF PHYSICIANS, INC.

Balance Sheet, December 31, 1930

ASSETS		
Cash in Bank and on Hand	\$43,277.20	
Bonds Owned (Schedule No. I)	43,036.70	
Accrued Interest on Bonds	302.92	
Inventory of Keys, Pledges, Frames, etc.	493.45	
	<u>\$87,110.27</u>	
Deferred Expenses for the Fifteenth Annual Clinical Session (Paid in Advance of 1931)	377.07	
Furniture and Equipment	\$3,227.80	
Less, Allowance for Depreciation	<u>291.78</u>	<u>2,306.02</u>
		<u>\$89,793.36</u>
LIABILITIES		
Deposits by Candidates, Applications Pending	30.00	
Deferred Income:		
Fifteenth Annual Clinical Session:		
Advance Collections for Exhibits	\$ 602.46	
Annals of Internal Medicine:		
Advance Subscriptions, Volume V	806.34	
Advance Subscriptions, Volume VI	<u>15.70</u>	<u>1,424.50</u>
Excess of Assets over Liabilities		<u>\$88,338.86</u>
FUNDS		
Endowment Fund (See Schedule No. II)	\$ 8,400.00	
General Fund (See Schedule No. III)	<u>79,938.86</u>	<u>\$88,338.86</u>

SCHEDULE NO. I

INVESTMENTS

December 31, 1930

Par Value	Bonds	Cost
3,000	Borough of Steelton, Pa., 4½s, 1933	\$ 3,071.25
5,000	Canadian National Railway 5s, 1969	4,987.50
2,000	Canadian National Railway 5s, 1969	2,055.00
2,000	Canadian National SS. Co. 5s, 1955	2,040.00
2,000	City of Detroit 4¼s, 1944	2,010.40
2,000	City of Houston 4¾s, 1942	2,077.50
1,000	City of Montreal 5s, 1956	1,071.30
2,000	City of Newark 4½s, 1944	2,075.00
10,000	City of Philadelphia 4½s, 1979	10,225.00
2,000	City of Toronto 5s, 1936	2,020.00
500	Oklahoma Gas & Electric Co. 6s, 1940	487.50
2,000	Province of Alberta 4½s, 1956	1,896.00
5,000	Province of Ontario 4½s, 1933	4,925.79
1,000	Province of Ontario 5s, 1942	1,052.26
2,000	Port of New York Authority 4½s, 1952	2,042.20
1,000	Township of Cheltenham 4¼s, 1943	1,000.00
<u>\$42,500</u>	Total Annual Yield 4.6%	<u>\$43,036.70</u>

SCHEDULE No. II

ENDOWMENT FUND, PRINCIPAL

For the year ended December 31, 1930

Balance, January 1, 1930	\$5,300.00	
Life Membership Fees Collected During the Year Ended December 31, 1930	3,100.00	
Balance, December 31, 1930	<u>\$8,400.00</u>	

SCHEDULE No. III

GENERAL FUND, PRINCIPAL

For the year ended December 31, 1930

Balance, January 1, 1930	\$60,624.07	
Less, Transfer to Endowment Fund of Initiation Fees of		
Life Members paid prior to January 1, 1930	800.00	\$59,824.07
Add, Net Income for the Year Ended December 31, 1930		20,114.79
(Schedule No. IV)		<u>\$79,938.86</u>

SCHEDULE No. IV

GENERAL FUND, INCOME AND EXPENSES

For the Year ended December 31, 1930

INCOME		
Annual Dues	\$24,698.80	
Initiation Fees	16,580.00	
Interest on Bank Deposits	1,461.06	
Income from Bonds Owned	1,218.18	
Income from Endowment Fund	411.00	
Profit from Sale of Keys, Pledges, Frames, Etc.	242.30	
Receipts from 1929-30 Directory	10.05	
Receipts from Annals of Clinical Medicine	11.30	
Total Income		\$44,632.69

EXPENSES

Fourteenth Annual Clinical Session:

Expenses:

Salaries	\$ 2,999.19	
Communications (Postage, Etc.)	394.14	
Stationery and Office Supplies	106.50	
Printing	1,179.63	
Traveling Expenses	3,149.89	
Auditorium Charges	746.56	
Honorarium	50.00	
Entertainment	409.50	
Advertising	857.05	
Reporting	422.49	
Badges	314.48	
Ladies Committee	174.06	
Banquet	394.89	
Miscellaneous	121.85	\$11,320.23

Forward \$11,320.23 \$44,632.69

College News Notes

1489

EXPENSES (Continued)

Forward	\$11,320.23	\$44,632.69
Deduct:		
Exhibits	6,900.90	
Guest Fees	1,046.00	7,946.90
Net Expenses		3,373.33
Annals of Internal Medicine:		
Expenses:		
Salaries	4,805.56	
Communications (Postage, Etc.)	1,045.85	
Stationery and Office Supplies	9.74	
Printing	13,742.50	
Traveling Expenses	25.08	
Miscellaneous	125.92	19,754.65
Deduct:		
Subscriptions:		
Volume I	\$ 32.55	
Volume II	55.12	
Volume III	635.94	
Volume IV	14,887.90	15,611.51
Advertising:		
Volume III	2,182.12	
Volume IV	1,361.37	3,543.49
Net Expenses		19,155.00
		599.65
Executive Secretary's Office:		
Expenses:		
Salaries	\$ 9,661.52	
Communications (Postage, Telephone, Etc.)	1,030.03	
Stationery and Office Supplies	682.26	
Printing	912.20	
Rent and Maintenance	3,127.71	
Traveling Expenses	2,728.69	
Annual Audit	150.00	
Premium on Surety Bond	20.00	
Miscellaneous	192.45	18,504.86
Treasurer's Office:		
Expenses:		
Salaries	470.00	
Communications (Postage, Etc.)	20.00	
Stationery and Office Supplies	30.00	
Traveling Expenses	109.95	
Annual Audit	50.00	
Premium on Surety Bond	100.00	
Miscellaneous	30.00	809.95
Annals of Internal Medicine Distributed Free to Life Members....	84.00	
1930 Supplement (Cost of Production and Distribution).....	823.33	
Depreciation on Furniture and Equipment	322.78	24,517.90
Net Income for the Year.....		\$20,114.79

ANNALS OF INTERNAL MEDICINE

COST ANALYSIS

(Revised to March 10, 1931)

			Number of Pages	
	Scientific Matter	News Notes Covers, etc.	Paid Advertising	Total
Volume II July, 1928 to June, 1929.....	1195	254½	98½	1548
Volume III July, 1929 to June, 1930.....	1133	248	163	1544
Excess pages, Volume II over Volume III..	62	6½	64½*	4
Circulation, Volume I.....	1803	*Excess, Vol. III.		
Circulation, Volume II.....	1999			
Circulation, Volume III.....	2446			

Volume II				Volume III				
INCOME:								
Subscriptions; segregated								
from dues at \$6 per mem-								
ber				\$10,080.00		\$11,184.60		
Direct subscriptions				2,210.02		3,725.80		
Gross Receipts				\$12,290.02		\$14,910.40		
Less Expenses				43.17	\$12,246.85	135.28	\$14,775.12	
(Refunds, etc.)								
Advertising:								
Gross Receipts				\$ 2,019.93		\$ 3,311.34		
Less Expenses				239.59	\$ 1,780.34	186.51	\$ 3,124.83	
					\$14,027.19		\$17,899.95	
EXPENDITURES:								
Salaries				\$ 3,709.88			\$ 4,274.89	
Equipment, Net				11.10				
Postage and Telephone				684.09			945.95	
Office Supplies				104.61			61.46	
Printing				\$11,365.28		\$12,795.62		
Less Repayment for Excess								
Illustrations				\$261.42		\$121.69		
Less Inventory of								
Stock				451.25	712.67	813.29	934.98	
					\$10,652.61		\$11,860.64	
Traveling Expenses				42.50			65.08	
Miscellaneous								
(Editor's Office:								
Copyright, etc.)				127.78			130.74	
Cost				\$15,332.57			\$17,338.76	
Volume II —Deficit								\$1,305.38
Volume III—Surplus								561.19

APPRECIATION OF THE OATH

The New England Journal of Medicine (April 23, 1931, p. 887) quotes editorially from the Oath Required of Candidates for Membership in the American College of Physicians and comments, in part, as follows:

"Here is a code of ethics which should be endorsed by every practitioner. * * * Its spirit and application, if generally observed, should have a definite influence in the solution of many of the problems before the public. If the public can be led to believe that this high standard is the underlying principle of service, there will be less criticism of doctors and irregular practice will be more generally discredited. The solution of the problems of the cults is in the hands of doctors."

Dr. Leon T. LeWald, (Fellow), Professor of Roentgenology, New York University, addressed the County Medical Society at Schenectady, New York, on Tuesday evening, May 5th, 1931. The subject was: "Paget's Disease (Osteitis Deformans). Summary of 73 Cases. Remarks on Endocrine Etiology. Relationship to Deafness. Unusual Manifestations (Tumor Formation) Lantern Slides."

Dr. Fred Meixner (Fellow) delivered the Pi Sigma Phi Lecture before the faculty of Bradley College, Peoria, Illinois, on March 16th. The subject was "Modern Aspects of Health Education."

Dr. H. Hilton Shreve Read (Associated), Atlantic City, N. J., presented two Clinics in April at the Jefferson Medical College, of Philadelphia, illustrating the practical procedures indicated in the care of diabetic patients in general practice. Dr. Read had charge of the Diabetic Clinic in connection with the Medical Dispensary of the Jefferson Hospital for six years.

Dr. Archibald L. Hoyne (Fellow), Chicago, has been appointed Associate Clinical Professor in the Department of Pediatrics of the University of Chicago.

Dr. Henry A. Christian (Fellow), Boston, Mass., addressed the William Harvey Society, April 10, on "The Old and New in General Practice."

Dr. N. Emmons Paine (Fellow), Newton, Mass., has been reappointed Chairman of the Board of Trustees of the Westboro State Hospital, and also re-elected Vice President and Member of Investment Bureau of the West Newton Savings Bank.

Dr. Louis Faugeres Bishop, Jr. (Fellow), New York, N. Y., has been elected a trustee of Rutgers University.

Dr. Dean B. Cole (Fellow), Richmond, Va., was re-elected President of the Virginia Tuberculosis Association at its recent meeting.

Dr. Sinclair Luton (Fellow), St. Louis, conducted a heart clinic at the recent meeting of the Union County Medical Society.

Dr. Luvia M. Willard (Fellow), Jamaica, N. Y., was recently elected to honorary membership in Alpha Omega Alpha, Cornell Chapter. Dr. Willard is also Pediatrician of the Postgraduate Medical School and Hospital of New York City.

Dr. Joseph B. Wolfe (Associate), Philadelphia, has been appointed Associate Professor of Cardiology at Temple University School of Medicine.

Dr. Linn J. Boyd (Fellow), New York, N. Y., is the author of the following articles which appeared in the March issue of the Journal of the American Institute of Homeopathy: "Diabetes Mellitus" and "The Diagnosis of Pernicious Anemia."

The following members of the College participated on the program of the Philadelphia Heart Association, May 18 to 21, inclusive, as indicated:

Dr. Ross V. Patterson (Fellow), Philadelphia—"A Rational Plan for the Diagnosis and Treatment of Heart Affections"

Dr. Edward J. G. Beardsley (Fellow), Philadelphia—"Problems Associated with Aortic Regurgitation"

Dr. Elmer H. Funk (Fellow), Philadelphia—"Acute Endocarditis"

Dr. Henry K. Mohler (Fellow), Philadelphia—"Heart Block"

Dr. Edward Weiss (Fellow), Philadelphia—"Congenital Heart Disease"

Dr. William Egbert Robertson (Fellow), Philadelphia—"The Diagnosis of the Failing Heart Muscle"

Dr. H. Brooker Mills (Fellow), Philadelphia—"Heart Disease in Children"

Dr. Joseph B. Wolffe (Associate), Philadelphia—"Coarctation of the Aorta"

Dr. E. B. Krumbhaar (Fellow), Philadelphia—"Demonstration of the Pathology of the Cardiovascular System"

Dr. John Eiman (Fellow), Philadelphia—"Anatomy of the Conducting System with Demonstration of Injection of the Purkinje System and Demonstration of Injection of Coronary System"

Dr. James E. Talley (Fellow), Philadelphia—"Cardiovascular Phenomena of Thyroid Disease"

Dr. S. Calvin Smith (Fellow), Philadelphia—"Demonstration and Discussion of Electrocardiography in Diagnosis and Treatment of Heart Disease"

Dr. Charles C. Wolferth (Fellow), Philadelphia—"The Relation of Cardiology to General Medicine"

Dr. David Riesman (Fellow), Philadelphia—"Some of the Difficulties in the Diagnosis of Mitral Stenosis"

Dr. Truman Schnabel (Fellow), Philadelphia—"Diet and the Gastro-intestinal Tract in Relationship to Cardiovascular Disease"

The following Fellows of the College addressed the one-day clinical and scientific program bearing upon tuberculosis sponsored by the Nebraska Tuberculosis Association at the State Hospital at Kearney, April 30:

Dr. J. A. Myers, of Minneapolis—"Childhood Tuberculosis"

Dr. Miles Breuer, of Lincoln, Nebr.—"Diagnosis"

Dr. Warren F. Pearce (Fellow), Quincy, Ill., presented cases of hyperthyroidism at an all-day clinical meeting held by the Adams County (Ill.) Medical Society on April 13, at Quincy.

Dr. Harold Swanberg (Fellow), Quincy, Ill., addressed the same meeting on "Pre-radium Treatment of Carcinoma of the Cervix"

The New England Health Institute, held at Portland, Maine, April 20-23, was addressed by the following Fellows of the College:

Dr. Robert B. Kerr, Manchester, N. H.: "Health Education of the School Child"

Dr. George W. McCoy, Washington, D. C.: "Contributions to Preventive Medicine from the National Institute of Health"

The eighty-five annual meeting of the Ohio State Medical Association was held at Toledo, May 12-13, under the Presidency of Dr. Chester W. Waggoner (Fellow), of Toledo. Guest speakers included Dr. Harry M. Hall (Fellow), of Wheeling, W. Va., who spoke on "The Doctor and Immortality."

Dr. Frederick A. Willis (Fellow), Rochester, Minn., addressed the tenth annual meeting of the Philadelphia Heart Association, April 15, on "Problems Underlying the Prevention of Heart Disease"

The annual meeting of the South Carolina Medical Association was held at Greenville, S. C., May 5-7, under the Presidency of Dr. Kenneth M. Lynch (Fellow), of Charleston.

Dr. William H. Mayer (Fellow), Pittsburgh, Pa., was one of the guest speakers at the annual meeting of the West Virginia Medical Association held at Clarksburg, May 19-21. Dr. Mayer's subject was "The Nervous Patient and the Practitioner."

Dr. Walter C. Alvarez (Fellow), Rochester, Minn., addressed the Central Tri-State Medical Society, April 30, on "Practical

Points in the Treatment of Gastro-Intestinal Diseases."

Dr. Felix J. Underwood (Fellow), President of the Southern Medical Association, recently appointed Dr. Walter Baumgarten (Fellow), St. Louis, a member of the Council from Missouri of the Southern Medical Association. Dr. Baumgarten succeeds Dr. W. McKim Marriott (Fellow), St. Louis, whose term has expired, and having served the constitutional limit, was not eligible for reappointment.

Dr. J. Stuart Pritchard (Fellow), Battle Creek, gave the first lecture, April 1, of a series of lectures on communicable diseases in progress at the Herman Kiefer Hospital, Detroit, under the auspices of the Wayne County Medical Society, in conjunction with the Urological, Dermatological and Tuberculosis Societies of Detroit. Dr. Pritchard's subject was "Clinical Symptoms of Tuberculosis."

Dr. Felix J. Underwood (Fellow), Jackson, Miss., spoke before the fifty-second annual meeting of the Louisiana State Medical Society, April 14-16, on "Appraisal of County Health Work Based on Reduction of Morbidity and Mortality."

Dr. Cyrus C. Sturgis (Fellow), Ann Arbor, Mich., conducted a Clinic on pernicious anemia at the fifty-eighth annual meeting of the Northern Tri-State Medical Association, which was held at Ann Arbor, April 14.

Dr. Anton J. Carlson (Fellow), Chicago, addressed a joint meeting of the New York Academy of Medicine and the New York Gastro-Enterological Society, recently, on "Motor Mechanism of the Large Bowel."

Dr. Walter M. Simpson (Fellow), Dayton, Ohio, delivered an address on undulant fever at the Summitt County (Ohio) Medical Society on April 7.

On March 31, Dr. George R. Minot (Fellow), Boston, addressed the Vanderbilt University School of Medicine and the Nash-

ville Academy of Medicine on treatment of anemia.

Dr. George E. Pfahler (Fellow), Philadelphia, spoke before the Philadelphia Roentgen Ray Society, April 2, on "Demonstration of the Lymphatic Drainage of the Maxillary Sinuses."

Dr. William Egbert Robertson (Fellow), Philadelphia, was the speaker at a Postgraduate Seminar of the Philadelphia County Medical Society, April 8; his subject being "Some Physiological Applications in Medicine."

Dr. James B. McElroy (Fellow), Memphis, delivered the Presidential address at the meeting of the Tennessee State Medical Association held at Knoxville, April 14-16.

Dr. William A. White (Fellows), Washington, D. C., addressed the American Red Cross, April 13-16, on "Therapeutic Value of Hospital Social Service."

Dr. Walter W. Palmer (Fellow), New York, N. Y., recently lectured at the School of Tropical Medicine of the University of Porto Rico.

Dr. Walter C. Alvarez (Fellow), Rochester, Minn., was one of the guest speakers at the eighty-fourth semi-annual meeting of the Southern California Medical Association held at Coronado Beach, April 17-11. Dr. Alvarez's subject was "Diagnosis of Gastro-Intestinal Diseases from the History."

New Life Member

Dr. Roscoe L. Sensenich (Fellow), South Bend, Ind., recently subscribed to the Endowment Fund of the College, thereby becoming a Life Member.

The following Fellows of the College participated on the program of the Oklahoma State Medical Association's meeting, May 11-13, at Oklahoma City:

Dr. John H. Musser, New Orleans—address

Dr. A. W. White, Oklahoma City—"Gastro-duodenal Ulcer, Medical Aspects"

Dr. Ray M. Balyeat, Oklahoma City—"Recent Advancement in Allergy"

Dr. Carroll M. Pounders (Fellow), Oklahoma City, delivered the Chairman's Address at the meeting of the Oklahoma Pediatric Society on May 11.

Colonel Charles F. Craig (Fellow), Asst. Commandant, Army Medical Center, Washington, D. C., has been elected a Corresponding Member of the Societe de Medicine & d'Hygiene Tropicales Egypte, and Secretary General of the Commission Scientifique d'etudes of the Federation Internationale des Societies de Medicine & d'Hygiene Tropicales, Paris.

Dr. E. J. G. Beardsley (Fellow), Philadelphia, addressed the Gloucester County (N. J.) Medical Society, April 16, on "The Importance of Routine Procedures to Insure Correct Diagnoses."

Dr. Bernard Langdon Wyatt (Fellow), Tucson, Ariz., has been elected by the Executive Council to active membership in the American Medical Editors' and Authors' Association.

Dr. Konrad E. Birkhaug (Fellow), Associate Professor of Bacteriology at the University of Rochester School of Medicine and Dentistry, has been elected a member of the Norwegian Academy of Sciences.

Dr. Ralph O. Clock (Fellow), New York, N. Y., was the principal speaker at the annual meeting of the senior classes of the Schools of Science and Technology of Pratt Institute, Brooklyn, on March 25. Dr. Clock's subject was "The Nation's Health," in which he emphasized the part played by chemistry in the development of medical science.

Dr. John Dudley Dunham (Fellow), delivered an extra-mural lecture to the Senior Class at Ohio State University, April 23, 1931. His topic was "Diseases of the Esophagus," illustrated by lantern slides.

Dr. Earle E. Mack (Associate), Syracuse, New York, was recently elected Secretary of the Onondaga Medical Society, and also Trustee of the Syracuse Academy of Medicine.

Dr. Oliver T. Osborne (Fellow), New Haven, Conn., is the author of an article entitled "Rising Tide of Narcotic Addiction Menaces Mankind" in the February 22, 1931, issue of the New Haven Register.

Dr. Samuel M. Feinberg (Fellow), Chicago, Ill., addressed the Saginaw (Mich.) County Medical Society, February 17, on "Allergy."

Dr. Carl V. Vischer (Fellow) of Philadelphia was recently elected Chief of the Medical Out-patient Department of Hahnemann Hospital, Philadelphia. Dr. Vischer is the author of an article, "Modern Advances in General Therapeutics," which appeared in the February issue of the Hahnemannian Monthly.

Dr. Howard T. Phillips (Fellow), Wheeling, West Virginia, is the author of a paper entitled "Use and Misuse of X-Rays in Skin Diseases" in the February issue of the West Virginia Medical Journal.

Dr. Will Gardiner (Fellow), Toledo, Ohio, was elected vice president of the staff at the annual meeting of the Women's and Children's Hospital of Toledo.

Dr. Ellen C. Potter (Fellow), Trenton, N. J., Director of Medicine of the Department of Institutions and Agencies, was appointed Chairman of the Program Committee of the New Jersey Conference of Child Health and Protection, called by the Governor as part of the follow-up program of the White House Conference.

The State Conference was held April 16-18 on the campus of the Woman's College at New Brunswick.

The first State Conference on Mental Hygiene for the State of New Jersey was held in Newark, February 27, under the auspices of the Mental Hygiene Committee of the State Board of Control. Dr. Potter presided

in the absence of Commissioner Ellis. The purpose of the conference, which brought together ninety-five psychiatrists, psychologists and psychiatric social workers, was to determine state policy in this field.

Dr. N. Worth Brown (Fellow), Toledo, Ohio, has been appointed Lieutenant Colonel of Medical Reserves, U. S. Army, attached to the 83rd Division and assigned to the Toledo Mobilization Center.

Dr. Thomas W. Durbin (Associate), Director of Medicine at the Flower Hospital of Toledo, Ohio, and Dr. N. Worth Brown (Fellow), Chief of the Medical Service of the Toledo Hospital, have joined the newly established "Toledo Clinic," a group which includes representatives from each special field in medicine and surgery, and which is associated through its members with the staff work of five Toledo hospitals.

Dr. George R. Minot (Fellow), Director of the Thorndike Memorial Laboratory, Boston City Hospital, addressed the Alpha Omega Alpha Chapter of Vanderbilt University Medical School at Nashville, Tenn., March 31, on "The Treatment of Anemia." Dr. Minot addressed the Harvard Medical Alumni Association, April 17, on the same subject.

Dr. Albert F. R. Andresen (Fellow), N. Y., read a paper on "Newer Aspects of Peptic Ulcer" before the Flatbush Medical Society on January 9, and on "Medical Treatment of Gastro-duodenal Ulcer," before the Queens County Medical Society on January 27.

Dr. Andresen also gave a popular lecture at the Prospect Branch, Young Men's Christian Association, under the auspices of the Public Health Committee of the Medical Society of the County of Kings, January 16, his subject being, "Constipation."

Dr. Curran Pope (Associate), Louisville, Ky., delivered a radio address over the radiophone of WLAP, Louisville, Ky., February 22, "George Washington, Soldier and Statesman."

Dr. Oliver T. Osborne (Fellow), New Haven, Conn., is the author of an article entitled "The Relation of Medicine to Dentistry" in the American Journal of Stomatology, January, 1931, page 43. Vol. IV, No. 2.

Dr. John Kerr Pepper (Fellow), Winston-Salem, N. C., was recently elected President of the North Carolina Radiological Society. Dr. William T. Rainey (Fellow) of Fayetteville, N. C., was elected vice president.

Dr. Charles J. Bloom (Fellow), New Orleans, addressed the Tangipahoa Parish Medical Society, April 2, on Infant-Feeding.

The Faculty of Medicine of Paris (The Medical School of the University) announces that, during June and July, 1931, a comprehensive series of postgraduate courses will be presented. The enterprise is conducted under the auspices of the Association for the Development of Medical Relations (the "A. D. R. M.") a commission sponsored by the French Government.

The work will be presented in the English language. Clinics, lectures and demonstrations will be conducted in the great hospitals of Paris, on a wide variety of topics, by the most eminent French clinicians. A nominal fee will be charged for each course. Upon the completion of each course, the student who qualifies will receive a certificate covering the work, signed by the professor in charge.

Detailed information may be secured by addressing direct, Professeur E. Hartmann, President, "A. D. R. M.," Faculty of Medicine of Paris, 12, Rue de L'Ecole de Medicine, Paris (6e) or, in the United States, Doctor Frank Smithies, 920 N. Michigan Avenue, Chicago, Ill.

GIFTS TO THE COLLEGE LIBRARY

Acknowledgement is herewith made of the receipt of the following publications by members of the College:

Dr. Walter M. Simpson (Fellow), Dayton, Ohio; 1 book, "Tularemia."

- Dr. Chas. Hartwell Cocke, (Fellow), Asheville, N. C.: 11 reprints,
 "Time and Tuberculosis"
 "Pneumothorax Therapy in Tuberculosis"
 "Pneumothorax Therapy—A Consideration of its Value and Apparent Neglect"
 "Early Pulmonary Tuberculosis"
 "Chronic Familial Hemolytic Jaundice or Banti's Disease"
 "Albumin in the Sputum in Tuberculosis: its Value in Diagnosis and Prognosis"
 "Massive Atelectasis"
 "Spontaneous Pneumothorax Following Artificial Pneumothorax, with Operation and Recovery"
 "Tuberculin"
 "Early Diagnosis of Pulmonary Tuberculosis—the Essential Factor in Prevention and Cure"
 "Vaccines in the Treatment of the Secondary Infection in Pulmonary Tuberculosis"
- Dr. William D. Reid (Fellow), Boston, Mass.: 1 reprint,
 "The Differential Diagnosis of Subacute Bacterial Heart Disease and Banti's Disease. Case Report"
- Dr. Karl Rothschild (Associate), New Brunswick, N. J.: 2 reprints,
 "Familiäres Auftreten von Polycythaemia Rubra in Verbindung mit Chorea Progressiva Hereditaria Huntington" (with H. Doll)
 "Die Chorea Huntington—Familie R."
- Dr. Elwood A. Sharp (Fellow), Detroit, Mich.: 1 reprint,
 "The Relation of Toxicity to Dosage of Tetrachlorethylene"
- Dr. C. F. Tenney (Fellow), New York City: 6 reprints,
 "A General Survey of the Visceral Neuroses" (with W. H. Squires)
 "Systemic Manifestations of Vincent's Infection"
 "Monilia Pneumonia"
 "Pernicious Anemia" (with Jos. Lintz, S. D. Jessup & Harlow Brooks)
 "Certain Clinical Observations on Gastric Ulcer"
- "Effects of Intravenous Injections of Acriflavine in Sepsis" (with Jos. Lintz).
- Dr. Philip King Brown of San Francisco, a guest speaker at the 1930 (Minneapolis) Clinical Session of the College, has also contributed the following reprints:
 "Peptic Ulcers—Diagnosis and Treatment"
 "Thoracoplasty in the Treatment of Pulmonary Tuberculosis"
 "The Cost of Private Practice"
- Dr. Miles J. Breuer (Fellow), Lincoln, Nebr.: 2 reprints,
 "The Fatigue Conscience in Tuberculosis"
 "Pulmonary Tuberculosis without Lung Symptoms"
- Dr. Edward E. Cornwall (Fellow), New York, N. Y.: 3 reprints,
 "Suggestions for the Dietetic Treatment of Heart Failure"
 "Arterial Peristalsis and Essential Hypertension"
 "A Primer of Pneumonia Therapeutics"
- Dr. Charles F. Craig (Fellow), Washington, D. C.: 12 reprints.
 "The Diagnostic Value of the Complement Fixation Test in Amebic Infections"
 "The Prophylaxis and Treatment of Amebiasis"
 "The Technique and Results of a Complement Fixation Test for the Diagnosis of Infections with *Endamoeba Histolytica*"
 "The Nuclear Structure of *Dientamoeba Fragilis*"
 "A Comparison of the Practical Value of the Wassermann and Kahn Tests in the Diagnosis of Syphilis in the Military Service"
 "Directions for Making the United States Army Typhoid-Paratyphoid 'A' Vaccine"
 "Observations Upon the Hemolytic, Cytolytic and Complement-Binding Properties of Extracts of *Endamoeba Histolytica*"
 "The Value of Cultural Methods in Surveys for Parasitic Amebae of Man"

- "A Simplified Method for the Cultivation of *Endamoeba Histolytica*"
- "The Relation of Officers of the Medical Corps to Scientific Medicine"
- "Observations Upon Complement Fixation in Infections with *Endamoeba Histolytica*"
- "Complement Fixation in the Diagnosis of Infections with *Endamoeba Histolytica*"
- Dr. Joseph R. Darnall (Fellow), Washington, D. C.: 5 reprints,
 "A Case of Chloroma of the Sacrum"
 "Modern Conception and Rational Treatment of Diabetes Mellitus"
 "Dietetic Management of Cardiac, Vascular, and Renal Disease"
 "The Application of Occupational Therapy to Chronic Medical Cases"
 "Diet in Heart and Kidney Disease"
- Dr. C. Ray Lounsberry (Fellow), San Diego, Calif.: 1 reprint,
 "Dermatological Neurosis"
- Dr. William D. Reid (Fellow), Boston, Mass.: 1 reprint,
 "Heart Murmurs in the Practice of Medicine"
- Dr. Lea A. Riley (Fellow), Oklahoma City, Okla.: 1 reprint,
 "A Surgical Diabetic"
- Dr. James S. Simmons (Fellow), Washington, D. C.: 22 reprints,
 "The Isolation and Cultivation of Tubercle Bacilli Protected from Light"
 "Dengue Fever"
 "Malaria on the Island of Corregidor, P. I."
 "A Malaria Survey at Fort Stotsenburg, P. I."
 "The U. S. Army Medical Department Research Board"
 "An Acidfast Organism Isolated from a Mouse"
 "Bactericidal Action of Mercuriochrome—220 Soluble and Iodine Solutions in Skin Disinfection"
- "The Intravenous Use of Acriviolet and of Mercurochrome in Bacterial Infections"
- "A Culture Medium for Differentiating Organisms of Typhoid-Colon Aerogenes Groups and for Isolation of Certain Fungi"
- "The Chronic Typhoid Carrier State Following Typhoid Infections in Vaccinated Individuals"
- "Negative Blood Cultures in Subacute Bacterial Endocarditis—Report of Two Cases"
- "A Comparison of the Schulte-Tigges and Ziehl-Neelsen Methods for Staining Acid-Fast Bacteria"
- "The Presence of Virulent Tubercle Bacilli in Human Bile"
- "Virulent Diphtheria Bacilli Carried by Cats"
- "Experimental Studies of the Treatment of Surra"
- "Observations on Equine Dhobie Itch of the Philippines"
- "The Use of Tetanus Antitoxin in the Protection of Horses Against Infection by *Clostridium Tetani*"
- "The Prevalence and Distribution of Malaria on the Island of Corregidor, P. I."
- "Bacteriological Data on the Chlorine Treatment of Respiratory Diseases"
- "Diphtheria Infections, with Particular Reference to Carriers and to Wound Infections with *B. Diphtheriae*"
- "Diphtheria Bacilli from Postoperative Empyema Wounds"
- "Dermatitis Venenata Produced by an Irritant Present in the Stem Sap of the Mango (*Mangifera Indica* L.)"
- Dr. Carl V. Vischer (Fellow), Philadelphia, Pa.: 1 reprint,
 "Modern Advances in General Therapeutics"

OBITUARY

CHARLES PRADFORD McABOY

Charles Bradford McAboy, Ph. B., M.D. (Associate), who was born in Butler, Pa., July 29, 1875, and was graduated from the University of Pennsylvania School of Medicine in 1901, died at his home in the East End, Pittsburgh, Pa., February 5, 1931, of cerebral hemorrhage. Dr. McAboy was physician to the Columbia Hospital, Wilkinsburg, was a valued member of his state and county medical societies, a Fellow of the American Medical Association, and had been an Associate of the American College of Physicians since 1923. With his modest and pleasing personality and his skill in the practice of his profession, Dr. McAboy had endeared himself to a wide circle, both among his patients and his fellow physicians.

Furnished by E. Bosworth McCready, F.A.C.P., Governor for Western Pennsylvania.